

A DISSERTATION ON
“THE EFFECT OF DEXMEDETOMIDINE
ON HEMODYNAMICS, POSTOPERATIVE SEDATION AND
ANALGESIA IN PEDIATRIC PATIENTS UNDERGOING
ADENOTONSILLECTOMY”

Submitted to

THE TAMIL NADU DR. MGR. MEDICAL UNIVERSITY,
CHENNAI-600032. TAMILNADU.

In partial fulfillment of the regulations

For the award of the degree of

M.D. DEGREE BRANCH-X
ANAESTHESIOLOGY



April 2016

GOVERNMENT MOHAN KUMARA MANGALAM
MEDICAL COLLEGE, SALEM, TAMILNADU

Ethical Committee Meeting held on 08.01.2015 at 11.00 A.M in the Seminar Hall, IInd Floor, Medicine Block, Govt. Mohan Kumaramangalam Medical College Hospital, Salem 01.

The following Members were attended the Meeting.

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9. Dr. Priya Jeyapal, MD., Professor and HOD of Biochemistry, Govt. Mohan Kumaramangalam Medical College, Salem.

Sl. No.	Name of the Presenter with Address	Title	Name of the Guide and Address	Whether it is Approved or not.
1.	Dr. S. Vijayakumar, II Year MD., P. G. Student, GMKMC, Salem – 30.	The effect of dexmedetomidine on hemodynamics, Post operative sedation and analgesia in pediatric patients undergoing adenotonsillectomy.	Dr. C. Santhana Krishnan, MD., Associate Professor of Anaesthesiology Department, GMKMC, Salem.	Approved

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ANALGESIA IN PEDIATRIC PATIENTS UNDERGOING
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A DISSERTATION ON

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LIST OF ABBREVIATIONS

HR – Heart Rate

SBP – Systolic Blood Pressure

DBP – Diastolic Blood Pressure

RSS – Ramsay Sedation Score

CHEOPS – Children’s Hospital of Eastern Ontario Pain Scale score

INTRODUCTION

Paediatric patients accounts for nearly 33% of all patients who undergo ENT surgery. Adenotonsillectomy is one of the frequently performed surgeries in children. Thorough knowledge of airway anatomy and its pathology of pediatric airway is essential for safe anaesthetic management. Safe management of pediatric anaesthesia always requires fluent proficiency in pediatric airway.¹ Utmost vigilance is required till the end of procedure since both anaesthesiologist and surgeon share the airway.

The Waldeyer's ring is the circle in the pharynx where the lymphoid tissues tonsil and adenoids are seen circling the pharynx. These lymphoid tissues develop during the 2nd yr of birth, start to grow and then regress progressively. The common symptoms seen with a patient with hypertrophy of adenoids include nasal obstruction, repeated infections, glue ear and sensorineural hearing loss. A person with recurrent tonsillitis with more than 5 episodes of sore throat in a year definitely forms an indication for Adenotonsillectomy.

Peritonsillar abscess, Obstructive sleep apnoea , Peritonsillar abscess are among the other indications for tonsillectomy. Hypertrophy of adenoids with sensorineural hearing loss, Obstructive sleep apnoea and nasal block requires adenoidectomy. A child with OSA will get 95 % relief from symptoms and quality of life when adenotonsillectomy is done.

In Obstructive sleep apnoea in children more than 6 yrs of age , upper airway function is disturbed with hypertrophy of adenoids and tonsils. Perioperative complications are increased in children with OSA and they require high dependency care and management. Laryngospasm, desaturation and airway obstruction are the recognized complications intraoperatively.

Loss of pharyngeal muscle tone, loss of ventilatory response to hypoxia, hypercapnia and airway obstruction are all the mechanisms by which anaesthetic drugs, sedatives and opioids exacerbate apnea.² Airway management, adequate analgesia and prevention of PONV are the vital areas where anaesthetist role is needed.

During airway management, difficult access of tonsil, airway sharing with ENT surgeon and airway soiling should be taken into consideration while giving anaesthesia.

Tonsillectomy is with high morbidity for increased post tonsillectomy bleeding, dehydration and postoperative nausea and vomiting. Inadequate pain relief and PONV account for readmission in children undergoing this surgery.³

Postoperative pain in tonsillectomy patients is a challenging concern for the anesthetist. Pain can be defined as “unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”. That too pain in pediatric population is something which is a complex idea. Differentiating the cause for pain in pediatric age group gives a wide range causes from pain to fear.

Successful pain therapy to change the physiological response has been viewed as an important branch of pediatric anaesthesia and surgery.⁴ Also the safety of analgesics are at stake like increased respiratory depression and poor recovery hesitates the anaesthetist in treating pain in pediatric age group.

Pain is very common after having the tonsils removed. Pain may occur in the throat or in the ears which usually radiates from the throat to the ear. The reason why patients experience pain is mostly due to absent strategy of analgesic management or unattended and decreased dose of analgesic rescue doses. For many years paracetamol and codeine has been the choice for postoperative pain relief in patients undergoing adenotonsillectomy.

NSAIDS for Analgesia:

Historically NSAIDS have been used to reduce the increased dose of opioid as tonsillectomy is associated with moderate to severe pain. The adverse effects of NSAIDS include torrential bleeding, decreased platelet count, status asthmaticus, tachycardia and sodium and water retention. However there is uncertainty regarding the use of non-steroidal anti-inflammatory drugs (NSAIDs) for pain control after tonsillectomy because of the concern for increased rates of bleeding. NSAIDs have been associated with increased bleeding rates since this class of drugs interferes with platelet aggregation, with a tonsillectomy carrying an inherent risk of bleeding of 1% to 5 %. Among the NSAIDS, ketorolac has got increased incidence of post tonsillectomy bleed.

Opioids for Analgesia:

The tolerance to pain is increased by opioid analgesics and these drugs form the foremost effective postoperative pain management in adenotonsillectomy patients. Narcotics can be safely used in patients more than 1 year of age. For acute treatment of pain, intravenous route is the best. The opioid related respiratory depression incidence is on the rise in children, alerting us to identify the high risk patients and other factors contributing to the same.⁶

The use of codeine is on the question, for it has caused increased number of fatalities, which is one of the most frequently used drug in analgesic management in adenotonsillectomy patients. This has made the research people to find a suitable alternative in the pain management of tonsillectomy patients. 3 cases of fatalities have been reported in recent papers who received codeine paracetamol after tonsillectomy in 2010 to 2011.⁵ The reason why it has fallen out of favor was due to the CYP2D6 polymorphisms.

Recent recommendations suggest routine administration of NSAIDS and paracetamol abandoning the opioid codeine. Also the correct dose and type of opioid for rescue analgesia studies are very limited.⁶

AIM AND OBJECTIVE

AIM OF STUDY

To study the effect of addition of Dexmedetomidine in Pediatric patients undergoing elective adenotonsillectomy for intraoperative hemodynamics, sedation and analgesia under General Anaesthesia.

OBJECTIVES OF THE STUDY

To compare the effects of addition of Dexmedetomidine to patients undergoing adenotonsillectomy under general anaesthesia.

The outcomes measured are

- ✓ Alteration in HR
- ✓ Alterations in SBP, DBP, MBP
- ✓ Post operative Analgesia and Sedation
- ✓ Emergence Delirium
- ✓ Nausea and Vomiting.

PEDIATRIC ADENOTONSILLECTOMY

ADENOTONSILLECTOMY remains one of the commonest surgical procedures carried out in pediatric age group. Historically, the chief indication was recurrent infection; however more and more children are now presenting with obstructive symptoms, and in the most severe of these cases, patients have frank obstructive sleep apnea syndrome.

INDICATIONS

It can be divided into absolute and relative indications

ABSOLUTE INDICATIONS

1. Airway obstruction.
2. Quinsy.
3. Acute on chronic tonsillitis with febrile seizures.
4. Tissue specimen.

RELATIVE INDICATIONS

1. Chronic tonsillitis not responding to drugs
2. Pharyngitis due to tonsillitis.
3. Chronic tonsillitis of more than 6 times a year.

4. Persisting symptoms of 1 or more years.

5. Distressing sore throat episodes

i. Constant halitosis and taste

ii. Chronic tonsillitis in streptococcus infection

iii. Neoplasm of biopsy

CONTRAINDICATIONS FOR SURGERY

1. Disorder of bleeding and infection.

2. Suppurative infection.

3. Low haemoglobin level

4. Increased risk for anaesthesia.

The age of most of the patients scheduled for tonsillectomy operation are less than 12 years and most of these children attend hospital on the day of surgery. During routine preoperative anesthetic evaluation of these patients, special emphasis is given on checking for loose tooth, recent ingestion of aspirin and determination of coagulation profile. The use of premedication is debatable in tonsillectomy operation, because some anesthetists like them and some do not. If premedication is given, it is administered most conveniently to the younger child as syrup of trimeprazine (1.5 mg/kg) or promethazine (1000

mcg/kg) or diazepam (200mcg/kg) or atropine (10-20 mcg/kg) orally and Triclofos 75mg/kg per oral.

The aims of different techniques of anaesthesia for elective tonsillectomy are

1. To provide deep anaesthesia that prevents reflex tachycardia arising from surgical stimuli in light plane of anaesthesia and cardiac arrhythmias. This is because one of the important intraoperative complications in tonsillectomy is arrhythmias which are caused by the increased levels of endogenous epinephrine from light general anaesthesia and sensitization of myocardium to this catecholamine.
2. To provide adequate muscle relaxation this will allow easy placement of mouth gag.
3. To prevent bucking, coughing or straining.
4. Rapid recovery to consciousness and also rapid return of protective airway reflexes.

Most of the children who are presented for tonsillectomy surgery are younger enough and allow an IV induction of anaesthesia. But in some children with poor venous access, inhalation induction may be preferred followed by IV access. Oral or nasal intubation is facilitated by succinylcholine or performed under deep inhalational anaesthesia.

Anaesthesia for tonsillectomy is usually maintained by using N₂O, non-depolarising muscle relaxants and narcotics with or without volatile anaesthetic agents. A topical spray of 4% lignocaine on tonsillar operative area or

infiltration of 2% lignocaine at surgical site will help to decrease the general anaesthetic requirements, the incidence of arrhythmias, and postoperative stridor and laryngospasm. Blood loss should be replaced, if it exceeds 1/10th of the total blood volume.

Tracheal extubation performed with patient's head slightly down in a lateral position, and after complete suction which ensures that the pharynx and larynx is free from blood secretions and tissue debris. Extubation may be done either under deep anaesthesia or when the patient is fully awake. When extubation is done under deep anaesthesia to prevent cough, vomiting, laryngospasm, etc., then the anaesthetist must continue to take the responsibility of protecting the airway after extubation too. Commonly trachea is extubated in the operating room when the patient is awake and protective airway reflexes have come back.

It results in some cough and laryngospasm which usually do not interfere with the surgical closure of tonsillar bed. Sometimes IV lignocaine (1 mg/Kg) may be used to decrease this laryngospasm after extubation.

After extubation, patient should be observed for any bleeding and for any airway obstruction in recovery room for at least 90 minutes in tonsillar position. This is done to make the blood or secretions to seep out of patients airway than into the larynx through vocal cords. Then the pharynx should be rechecked directly for bleeding.

The risk of nausea and vomiting can be as high as 70% during the first 24 hours after tonsillectomy. Although, post-operative bleeding is the most serious

complication, but persistent vomiting and poor oral intake are the most common cause for readmission after discharge. To reduce the incidence of post tonsillectomy (postoperative) vomiting, it is important to modify some anaesthetic techniques and also to develop some recovery protocol, such as avoidance of narcotics as postoperative analgesic, emptying of stomach from blood by suction, administration of antiemetic regimen, proper hydration and never force early oral food or fluid intake, etc.

Background Of Sevoflurane in Pediatric Adenotonsillectomy:

Sevoflurane is an inhaled volatile anaesthetic that a revolutionalised pediatric anaesthesia for induction and maintenance. It was first described by Wallius in 1975. It was first used in Japan in 1992 and later became widespread throughout the world by 1995. Due to its sweet smell, it makes induction and emergence has been very rapid. The postoperative behavioural concerns has been a problem with sevoflurane.

This behavioral disturbance has been described as Emergence agitation. It occurs during the recovery of the patient from anaesthesia with a wide variety of clinical signs like agitation, delirium, delusion, hallucinations, thrashing movements, involuntary movements, etc.,³⁸

No single scale has been universally accepted to grade the degree of emergence agitation. Some of them include “PAED scale”, “modified PAED scale”, etc.

The cause for Emergence agitation is unknown. Most of the symptoms of Emergence agitation is short lived but few patients have prolonged symptoms which necessitate pharmacological treatment and physical restraints.

Many surgeries have been implicated in the development of Emergence agitation, with Ent and Ophtalmological surgeries having the highest incidence.

Dexmedetomidine apart from its analgesia and sedative effects has also been found to decrease the incidence of “Emergence agitation” in patients undergoing adenotonsillectomy under Sevoflurane anaesthesia.

PAEDIATRIC POSTOPERATIVE SEDATION

Unconsciousness, sudden episodes of desaturation, upper airway obstruction, bronchospasm, laryngospasm and cardiac arrest are some of the side effects seen with pediatric sedation.

GOALS OF PEDIATRIC SEDATION

- ✓ Minimize physical discomfort and pain
- ✓ Guard the child's safety and welfare
- ✓ To reduce the anxiety and mental trauma
- ✓ Immobilization during surgery
- ✓ Safe discharge from medical supervision

GUIDELINES FOR SEDATION

1. Presedation assessment and preprocedural evaluation
2. Administration and titration of sedatives, hypnotics and analgesics based on the age of the child and comorbidities
3. Monitoring and Documentation during and after sedation
4. Availability of emergency equipments and medicines

5. Availability of supplemental oxygen source

6. Recovery care and discharge criteria

PRESEDATION ASSESSMENT

1. **EXPERIENCE:** Previous experience of the patient to be sedated should be asked for along with the unpleasant experiences and drugs used.

2. **MILESTONES:** The requirements of neurologically disabled children will be drastically reduced compared with a child with normal milestone or the chronological age than a similar patient with normal motor and social developmental. Children with congenital abnormalities need special care

3. **CARDIAC:** The functional reserve and detailed knowledge about the pathophysiology of specific congenital heart disease needs to be evaluated as all the drugs given can cause vasodilatation and or stimulation of the sympathetic nervous system that can result in cardiac failure and reversal of shunts in these children.

4. **PULMONARY:** Children with active respiratory infections and asthma which is poorly controlled can be postponed as they are more prone for respiratory complications.

5. **ASPIRATION:** The risk of aspiration in each child should be assessed with regard to duration of fasting, presence of gastroesophageal reflux disease, excessive drooling of saliva to prevent aspiration during sedation.

6. AIRWAY ASSESSMENT: Airway should be evaluated in detail which starts with good history from parents regarding noisy breathing, pattern of sleep and position related breathing problems in child with regurgitation of feeds related to pharyngeal dysfunction and anatomical defects in airway.

The size of the tongue in relation to the oral cavity, the degree of tonsillar enlargement are graded as follows

TONSIL GRADE:

- 0- Tonsil fit within tonsillar fossa
- 1- Tonsils < 25% of space between pillars
- 2- Tonsils < 50% of space between pillars
- 3- Tonsils <75% of space between pillars
- 4- Tonsils >75% of Space between pillars

RED FLAGS OF SEDATION

- ✓ Congenital heart disease with poor contractility/hemodynamic instability
- ✓ Apnea
- ✓ Preterm compromise of airway
- ✓ Adverse reaction to sedation previously
- ✓ Possibility of difficult air way
- ✓ GERD

- ✓ Loss of muscle tone
- ✓ Tremors
- ✓ Recent Pneumonia

Scales used for Sedation

“MICHIGAN SEDATION SCALE”

Score	Patient state
0	Awake/alert
1	Minimally sedated: Tired/sleepy, appropriate response to verbal conversation and/or sounds
2	Moderately sedated: Somnolent/sleeping, easily aroused with light tactile stimulation
3	Deeply sedated: Deep sleep, arousable only with significant physical stimulation
4	Unarousable

“RAMSAY SEDATION SCALE”

If Awake

Ramsey 1

Anxious, agitated, restless

Ramsey 2

Cooperative, oriented, tranquil

Ramsey 3

Responsive to commands only

If Asleep

Ramsey 4

Brisk response to light glabellar tap or loud auditory stimulus

Ramsey 5

Sluggish response to light glabellar tap or loud auditory stimulus

Ramsey 6

No response to light glabellar tap or loud auditory stimulus

PAEDIATRIC POSTOPERATIVE ANALGESIA

The concept of postoperative pain management and its use in pediatric age group has showed a dramatic improvement in recent years despite a universally accepted proper protocol. The usual misconceptions include that a child will experience less pain, he/she will get used to pain and is at increased risk of respiratory depression.

Regardless of age all pediatric population experience pain and it should be dealt with utmost care to prevent any unpleasant experiences during or after surgery. It has been demonstrated that even a premature neonate has a developed anatomical and physiological components that shows stress response to a painful stimuli. An unattended and unrelieved pain in children can prime them for chronic pain and also affect their psychosocial development.

Mechanism of pain:

Myelination of nerve pathways is always not essential for pain transmission. However, the conduction velocity will be slow which is offset by the shorter distances. Inhibitory pathways of pain develop in later decades. The Spinal cord's descending pathway is associated with inhibition of pain sensation. These are also developed later in life.

Physiological Signs of Pain in Children

- ✓ Tachycardia

- ✓ Tachypnoea
- ✓ Respiration becomes shallow with rapid desaturation
- ✓ Incessant cry
- ✓ Flushing
- ✓ Sweating of face and palm
- ✓ Changes in ECG

Some of the behavioral changes associated with pain include vocalization, muscle rigidity or flaccidity, making of fists, thrashing movements, changing agitation cycles, facial expressions, etc.

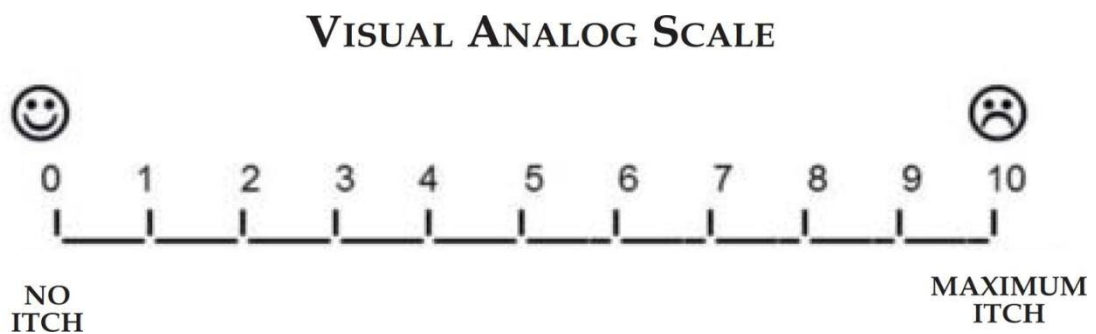
Assessment of Pain in Children:

Assessment of Pain in Children is very difficult because there is no ideal ubiquitously accepted technique. All the objective assessment techniques mainly rely on the physical signs of the sympathetic nervous system combined with behavioral assessment. There is always difficulty in differentiating the behavioral changes associated with pain from parental separation, anxiety or fear.

Since pain is a subjective experience, any self assessment scale is preferred to an observer's objective assessment.

A wide range of pain rating scales have been devised. Some of them are as follows

- 1. Numerical scales**
- 2. Simple descriptive scales**
- 3. Visual Analogue scale**
- 4. Wong Baker Face pain rating scale**
- 5. ‘Oucher’ scale**

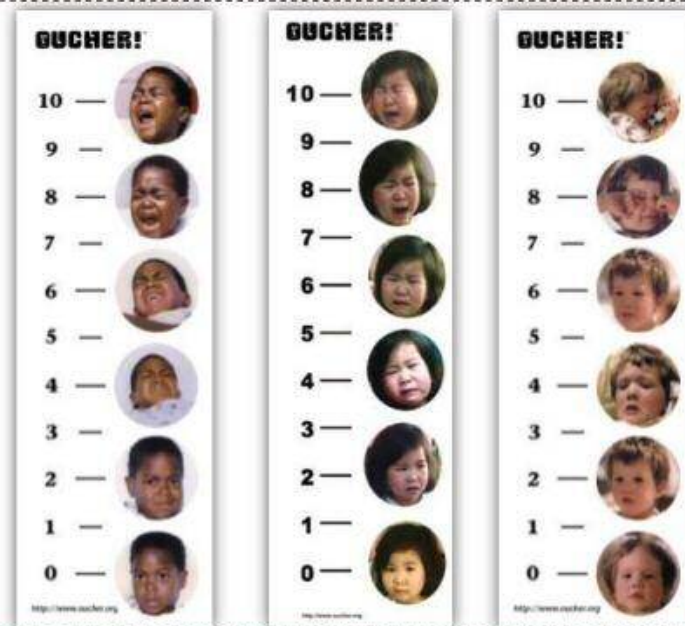


Wong-Baker FACES™ Pain Rating Scale



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Examples of the OUCHER Scale



Pain Management Strategies:

The analgesia plan should always be decided before inducing anaesthesia since consent is required for certain procedures. Few analgesic techniques will improve in the postoperative period when a preoperative teaching is made.

The anatomical consideration, surgical procedure, physical and mental development of the child should always be kept in mind while planning for a postoperative analgesia. The type of surgical procedure is the most important determinant in choosing the technique of postoperative pain management. Superficial surgeries require decreased needs compared to invasive surgeries.

The incorporation of the method of postoperative pain management in the anaesthesia plan makes sure that the child gets adequate pain relief during surgery, volatile used is decreased and the child emerges without pain. It has been found that to maintain analgesia in a child without pain is easy compared to a child emerging with severe pain from surgery.

Treatment strategies for Postoperative pain:

1. Mild pain should be treated with NSAIDS
2. Moderate pain should be treated with NSAIDS, NSAIDS combined with opioids, Intravenous bolus of opioids, continuous infusion of opioids or a regional anaesthetic technique

3. Severe pain is treated by intravenous bolus of opioids or a regional anaesthetic technique

Common Modalities of Pain management in Pediatric population:

a. Non Opioid Analgesics

- Paracetamol
- Nsaids
- Alpha 2 Agonists

b. Opioid Analgesics

c. Regional Anaesthetic Techniques

- Central Neuraxial blockade
- Peripheral nerve blockade

d. Cognitive behavioural techniques

NON OPIOIDS:

1.Paracetamol:

This is the most commonly used drug for mild to moderate pain and as an adjunct for severe pain. The oral dose of this drug is 10-15 mg/kg 4th hourly to a maximum of 100 mg/kg for children below 12 yrs of age. The rectal dose is 35-40 mg/kg and repeat dose is 20 mg/kg every sixth hourly.

2.NSAIDS:

The increased safety margin and decreasing the requirement of the opioids make NSAIDs the right choice for immediate postoperative pain relief. The most commonly used NSAIDs include Ibuprofen(6- 10 mg/kg) fourth hourly, Naproxen 5- 10 mg/kg 12th hourly, Ketorolac 0.5 mg/kg 6th hourly. Compared to adults, the side effects of NSAIDs in children, like gastrointestinal bleeding, renal side effects are less. But the increased risk of bleeding is seen in children undergoing tonsillectomy surgery. Hence, they should be used with caution or avoided in such surgeries for postoperative pain relief.

3. Alpha 2 agonist:

These are the new class of drugs emerging as a premedicant, analgesic and sedatives. The mechanism of action is in the locus ceruleus of brain. The most commonly used drug is clonidine. As a premedicant, it is used in a dose of 4 mcg/kg. The anaesthetic sparing effect of clonidine was found to decrease

the postoperative analgesic requirements. However, the hemodynamic instability caused by clonidine has offset many people to avoid using it judiciously. Another alpha 2 agonist which has similar effects of clonidine is dexmedetomidine, whose off label use in pediatric patients is increasing now a days.

OPIOIDS

Traditionally opioids are considered as the first line in the management of severe pain. Within the therapeutic blood values of opioids, these drug can be used without the fear of respiratory depression or over sedation. There are three choices during opioid delivery which should be selected for postoperative analgesia.

1. Type of opioid to be used
2. Mode of administration
3. Route of administration

The best opioid for postoperative analgesia is still on the study. There are acceptable alternatives which are available providing equipotent analgesia. The options available for mode of administration include intravenous bolus when needed, intermittent administration, continuous administration or patient controlled analgesia. At anytime, the serum levels should be within the therapeutic range for the fear of its side effects.

The common route of administration include intravenous, intramuscular, subcutaneous, epidural or caudal. Intramuscular route is very unpleasant with incalculable uptake. Intravenous i.v bolus given intermittently appears to be the best route for quick onset and relief of pain. The patient controlled analgesia has the advantage of titrating the need of analgesia by allowing the patient to administer small doses using a microchip pump. It is successfully used only if the child is above 7 yrs of age.

The most commonly used opioids are morphine and fentanyl. The iv doses in children in morphine is 50-100 mcg/kg and that of fentanyl is 0.5-1 mcg/kg.

Adverse effects of Opioids:

1. **Respiratory depression** – Discontinue the use of opioids and management of airway. Opioid antagonist like naloxone (2 mcg/kg) can be given.

2. **Constipation.**

3. **Nausea and vomiting** – Antiemetic like Promethazine(0.25mg/kg), droperidol and Ondansetron can be used.

4. **Pruritus** – Diphenhydramine can be given.

The sophistication of anaesthetic equipment and safe regional anesthetic techniques has improved the quality of analgesia. The most commonly used local anaesthetics in regional or nerve blocks include lignocaine, bupivacaine, ropivacaine, levobupivacaine ,etc.

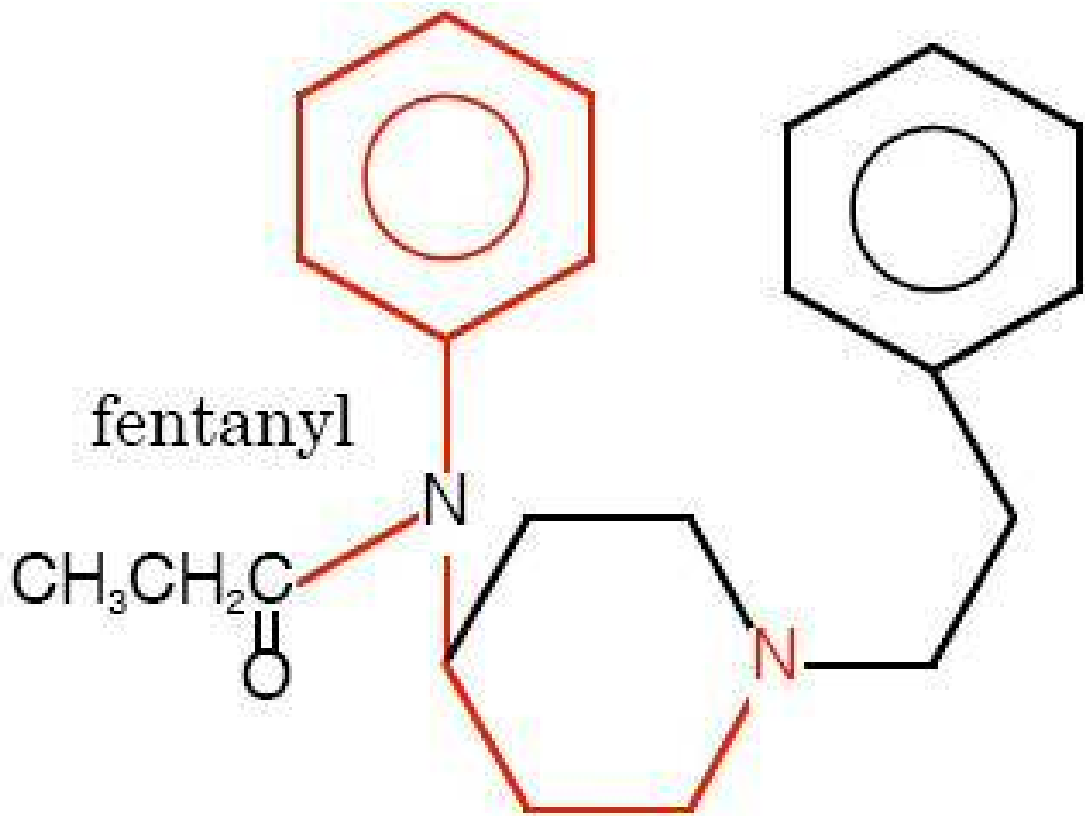
Various other complementary techniques like Distraction, Relaxation , Preparation and Rehearsal should be targeted to the individual needs of the child taking into account the age, gender, cognitive development, etc.

The sound knowledge about physiology of pain and better understanding of the pharmacology will provide the treating physician wide variety of options to provide pain relief in pediatric population. In addition, discovery of new drugs and new techniques is improving the quality of postoperative pain management.

PHARMACOLOGY OF FENTANYL

Structure :

Fentanyl is synthetic amine opioid which is structurally related to phenyl piperidine nucleus. It is pure mu receptor agonist and approximately 100 times more potent than morphine in term of analgesic dose.



Mechanism of Action:

Fentanyl acts on morphine or mu receptors, located in the cerebral cortex, thalamus, hypothalamus, corpus striatum, etc causing analgesia, respiratory depression, euphoria, miosis, reduced GI motility and physical dependence. It has no action on other opioid receptors namely kappa and delta receptors.

Pharmacokinetics:

Unlike morphine, the pharmacokinetics of fentanyl is described by a three compartmental instead of two compartmental model. The first pass uptake of fentanyl by lungs is 75 percent. The Pka is 8.4. So the unionized form of fentanyl is very less (<10%) compared to the ionized form. The volume of distribution of fentanyl is very high, which is explained by its high lipid solubility. The resultant effect of these two properties makes fentanyl to have a rapid onset of action. The protein binding capacity of fentanyl is 80%.

Metabolism:

Metabolism of fentanyl is liver enzymes by hydroxylation and dealkylation. The hepatic extraction ratio of fentanyl is very high. The major metabolite of fentanyl, Norfentanyl is seen in urine for up to 2 days after single iv bolus administration. It is inactive and has no analgesic property. The elimination half life of fentanyl is 1.5 to 2 hrs.

Dose:

Adults:

- For premedication – 50 -100 mcg (1-2 mcg/kg)
- Induction or supplementation of general anaesthesia – 1-100 mcg/kg
- Spinal and Epidural adjuvant – 25 – 50 mcg

Pediatric dose:

- Oral transmucosal – 10-15 mcg/kg
- Intranasal – 1-2 mcg/kg
- Transdermal – 25,50,75,100 mcg/hr patches
- Iv bolus – 0.5- 1 mcg/kg every 1-2 hrs
- Iv infusion – 0.5 mcg/kg

A small dose of fentanyl given will last for 30 – 60 minutes. When high doses are given, it may be effective up to 4 – 6 hrs. The cardiovascular stability of the drug is explained by the rapid onset and rapid termination of action when small boluses of drug are given.

EFFECTS:

All the effects produced are its action on mu or morphine receptor. Chest muscle rigidity, also called as “wooden chest phenomenon”, which is most

commonly seen after fentanyl administration is centrally mediated and may be due to its action on mu receptor, located on GABA nergic interneurons. This can be prevented by slow administration of the drug, diluting the drug before administration or pretreatment with other anaesthetic agents like i.v inducing agents(propofol, thiopentone). Neuroexcitation is a rare phenomenon seen in cases where high dose of fentanyl is given.

The adverse cardiovascular effects of fentanyl is bradycardia which is of vagal in origin. Cardiac output, Mean arterial pressure, Systemic vascular resistance, Pulmonary vascular resistance and Pulmonary capillary wedge pressure are either decreased or totally unaffected after administration of fentanyl. Studies have also shown that fentanyl the cardiovascular response to intubation is obtunded by fentanyl.

Fentanyl is a potent respiratory depressant opioid which causes decrease in both the respiratory rate and tidal volume. The ventilatory response to hypoxia and hypercarbia is diminished. It is also an antitussive agent and causes meager release of histamine. Thus, bronchospasm is very rarely produced by this drug.

The potency of fentanyl is about 100 times more than that of morphine. The hypnotic and sedative actions are less compared to other opioids. Miosis is produced as a result of stimulation of Edinger Westphal nucleus. Several reports of seizure activity has been reported in patients who receive fentanyl. However no “spike wave patterns” have been demonstrated after the use of fentanyl.

Gastrointestinal motility and gastric acid secretion is reduced by fentanyl. By causing spasm of sphincter of oddi it doubles the CBD pressure. Fentanyl also increases the tone of ureters, detrusor muscle of bladder and vesical sphincter. The metabolic response to stress and intubation stress response is obtunded by the use of high dose of fentanyl. ADH activity is not increased by fentanyl, which is seen with the use of morphine.

The MAC value of volatile anaesthetics is decreased by fentanyl like other opioids. The action of non depolarising skeletal muscle relaxants is also augmented by fentanyl. Fentanyl should never be mixed with sodium thiopentone as both these drugs are pharmaceutically incompatible.

The high lipid solubility of fentanyl makes it cross the blood brain barrier very rapidly and plasma CSF equilibrium is attained within 5 minutes of time. The concentration of fentanyl then starts to rapidly decrease in plasma and CSF due to redistribution of it from low volume but highly perfused group of tissues like brain to high volume but poorly perfused tissues like muscle and adipose tissues. The duration of action of fentanyl of a single bolus of fentanyl is low due to its rapid redistribution to other tissues rather than the metabolism and excretion of the drug by liver and kidney respectively. So fentanyl has a pharmacokinetics similar to that of the i.v inducing agents like propofol, thiopentone or ketamine. When saturation and equilibrium of the high volume less perfused tissue occurs, then the effects of fentanyl are prolonged with elimination half life of around three to four hours.

DRUG INTERACTIONS:

The analgesic concentration of fentanyl augments the action benzodiazepines. Synergism is seen with ventilatory depression and hypnosis. In clinical practice, this synergy between benzodiazepines and opioids is carefully against the adverse additive depression of ventilation and delayed recovery.

SIDE EFFECTS:

1. Cardiovascular Effects: As the release of histamine is very less when compared to other opioids, bradycardia is more prominent with fentanyl which leads to decrease in cardiac output and blood pressure.
2. Epileptic Fits: EEG is always essential to differentiate seizures from myoclonus like activity or skeletal muscle rigidity due to fentanyl.
3. Intracranial pressure: Modest increase in intracranial tension is seen with fentanyl inspite of keeping PaCo₂ constant

CLINICAL USES:

- Analgesia – (1-2 mcg/kg IV)
- As an adjuvant to inhaled volatile agents to blunt the intubation response or sudden increase in surgical stimulus
- To decrease the dose of inhaled agents needed to blunt the intubation response

- Surgical Anaesthesia (100-150mcg/kg IV)
- Labour Analgesia (25-50 mcg intrathecally)
- Transmucosal preoperative medication
- **Post operative analgesia**

PHARMACOLOGY OF DEXMEDETOMIDINE

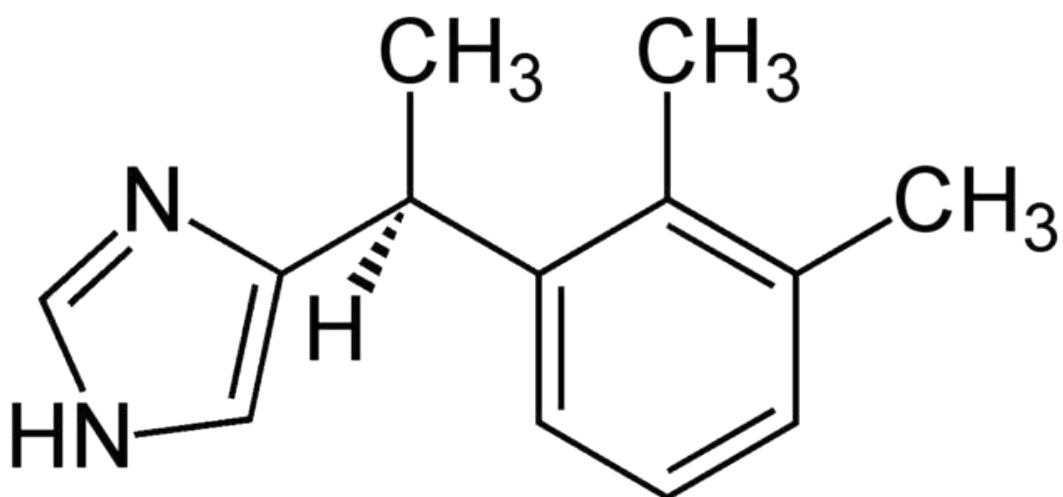
Dexmedetomidine (Dex) has made its foray in India very recently. It has gained wide popularity as an adjunct to the anaesthetist armamentarium

CHEMISTRY:

Dexmedetomidine is a selective alpha 2 adrenoreceptor agonist which was developed as an alternative to clonidine. The prototypical alpha 2 adrenoreceptor agonist is clonidine. Alpha 2 adrenoreceptor agonists have several beneficial effects like

1. Anxiolysis
2. Analgesia
3. Sedation
4. Sympatholysis

Dexmedetomidine, alpha 2 adrenoreceptor agonist, is made up of imidazoline structure. Dexmedetomidine is the chemically active D-enantiomer of medetomidine, a substance which was used in veterinary medicine for long years. Compared with clonidine, dexmedetomidine is roughly eight times more specific for alpha 2 receptors



Alpha adrenergic receptors:

The adrenergic receptors are widespread in our human body. The endogenous catecholamines like Adrenaline, Dopamine, etc act on these receptors. These receptors also mediate the clinical effects of many other drugs. A total of 9 adrenergic receptors have been synthesized so far. They include three alpha 1, three alpha 2 and three beta adrenergic receptors. Alpha 2 receptors have been implicated in variety of physiological functions.

The alpha 2 adrenoreceptor subtype is predominantly discovered in brain which mediates functions like sedation, anxiolysis, analgesia and also in behavioural changes. When alpha 2b Adrenoreceptors are stimulated, it causes vasoconstriction and systemic hypertension. The alpha 2 a receptors are responsible for causing hypotension . Hypothermia and behavioral changes are produced by alpha 2c subtype. Thus, the action of dexmedetomidine is varied

with no specificity to the particular alpha 2 receptors and it was a wide variety of actions

Mechanism of Action:

Alpha 2 receptors belong to the G protein coupled receptors. They are made up of 7 transmembrane helices. By coupling uncoupling mechanisms, the physiological response is produced. The proposed mechanisms include decrease of adenylyl cyclase which inhibits opening of the voltage gated calcium channels causing hyperpolarisation

Dose:

Dexmedetomidine is usually available in 2 ml containing 100 mcg/ml. It is usually given as an infusion dose of 1mcg/kg over 10 min followed by maintenance of 0.2-0.7 microgram/kg.

Distribution Metabolism and Elimination:

Dexmedetomidine is 95 % protein bound but does not displace any drug nor does it get displaced by any other drug. It is metabolized in the liver by glucuronidation and cytochrome P-450 mediated metabolism. It is eliminated by the kidney. Dose adjustment will need to be made in patients with liver impairment. No dose change needs to be made in patients with renal dysfunction.

Drug interactions:

Drug interactions of dexmedetomidine are many. The serum level of dexmedetomidine is increased by CYP2A6 inhibitors such as isoniazid, methosxalen and micaonazole, thus increasing the action of dexmedetomidine. On the other hand, it increases the level of CYP2D6 substrates like tricyclic antidepressants, beta blockers, lignocaine, etc. Side effects of dexmedetomidine like bradycardia and hypotension may be increased by vasodilators and beta blockers.

DURATION OF ACTION:

The half life of dexmedetomidine is 6 minutes and an elimination half life of two hrs.

ADVANTAGES:

Dexmedetomidine is a sedative and analgesic produces sympatholysis without any respiratory depression. This is useful in patients particularly in patients where sedation is required but depression of ventilation is not desirable. It is also an antisialagogue

CLINICAL USES**1. ICU SEDATION:**

Dexmedetomidine is used as an infusion in ICU patients for sedation and analgesia. It does not cause respiratory depression but cause moderate

reduction in blood pressure and heart rate. Caution should be used exercised in patients with severe ventricular dysfunction and advanced heart block

2. REGIONAL ANAESTHESIA:

Dexmedetomidine is administered in dose of 0.2 mcg/kg/hr along with infusion of Remifentanyl and propofol as required as adjunct to placement and management of regional anaesthesia including nerve blocks. Respiration is preserved with dose along with hemodynamic stability without the need of additional opioids. The depth of analgesia is increased and the additional need of analgesic supplements is drastically reduced when dexmedetomidine is used in regional anaesthesia

3. AWAKE FIBREOPTIC INTUBATION:

Patients cooperation is a vital parameter while performing awake fibreoptic intubation. At the same time, spontaneous respiration should maintained throughout the procedure. The discovery of dexmedetomidine is real boon for these type of off theatre procedures where access to the anaesthetist is very limited. Dexmedetomidine causes preservation of spontaneous breathing and also sympatholysis. These benefits have been exploited during fibreoptic intubation. There has been also reports that dexmedetomidine reduces secretions of oral airway which also supplements to the need of awake intubation.

Along with small doses of opioids and benzodiazepines with minimal dose of dexmedetomidine is used for awake airway intubation. Upper airway blocks can be supplemented to this to increase the plane of anaesthesia. The preservation of spontaneous respiration, sympatholysis, sedation, and analgesia of dexmedetomidine makes a better alternative for many other drugs .

4. TOTAL INTRAVENOUS ANAESTHESIA

Dexmedetomidine is used as the main TIVA on the airway where spontaneous ventilation needs to be maintained, access to airway may not be easily possible and rapid awakening may be required.

5. MONITORED ANAESTHESIA CARE

Dexmedetomidine can also be used to provide sedation for procedures done under monitored anaesthesia care where access to airway may not be easily possible and rapid awakening may be required.

6. CARDIOTHORACIC SURGERY

Dexmedetomidine is being used as supplement to anesthetic in patients undergoing cardiovascular and thoracic procedures. It is also being used as alternative to thoracic epidural in patients in whom it is contraindicated.

7. NEUROSURGERY

In Neurosurgery, intermittent deep and superficial plane of anesthesia is required during awake craniotomy surgeries. These are all provided by

dexmedetomidine. Lack of Delayed emergence, better hemodynamics and hypotensive anaesthesia are all provided by dexmedetomidine. It can cause decreased blood flow to intracranial cavity. Dexmedetomidine is also used for surgeries of spinal cord.

8.MEDIASTINAL MASS

Mediastinal biopsies and radiotherapy are done under sedation with the help of dexmedetomidine. The loading dose of is used is 1 mcg/kg/hr for 10 min and then 0.2-0.7 mcg/kg/hr maintenance infusion. Dexmedetomidine is safe as it does not depress respiration or the cardiovascular system and yet provides the required sedation

REVIEW OF LITERATURE

Vilo et al studied the effect of dexmedetomidine in pediatric population. Dexmedetomidine was initially introduced for sedation in adult patients in high dependency care unit. It was also indicated for use in sedating non intubated patients either before or during surgeries and also for medical procedures. The uses of dexmedetomidine include sedation, anxiolysis, analgesia and sympatholysis. The striking property of this drug is that it does not blunt the ventilatory drive. All these outstanding features make this drug as an alternative for pediatric procedural sedation and for ICU care. Although this drug is approved only for the use in patients on ventilators, the off label use of this drug in pediatric age group is increasing.⁷

Dexmedetomidine is of particular benefit in neurologically crippled children who don't tolerate sedatives like benzodiazepines. Hypotension and bradycardia are the most common side effects reported which was reported in up to 20 percent of subjects, which resolved with the reduction in dosage.⁷

Munoz et al showed that in those receiving midazolam or morphine, the dose of dexmedetomidine got reduced. The drug has high volume of distribution and protein binding capacity. The pharmacokinetics was linear within the dose of 0.2-0.7 mcg/kg/hr. It was metabolized mainly by the liver enzymes, CYP enzymes by hydroxylation and glucuronidation. Aliphatic hydroxylation produced the active metabolites and glucuronidation the inactive metabolites.

All the metabolites are excreted predominantly in the urine, with minor excretion in the feces. The author also concluded that the dose of the drug should be reduced in liver cirrhosis or end stage liver disease.⁸

Petroz et al was the pioneer who first studied the pharmacology of dexmedetomidine in children. It was published in the year 2006. Their study had thirty six subjects (age 2-12 yrs) divided into four groups, with three groups receiving the dexmedetomidine infusion (2, 4, 6 mcg/kg/hr) for 10 min and the other group received a placebo. All the pharmacokinetic and pharmacodynamic variables were derived. The drug had high protein binding capacity of around 93% and volume of distribution. The elimination half life was 2 hrs.⁹

Diaz et al after one year studied the drug's pharmacokinetics in children who underwent surgery and monitored in ICU. He too published similar reports to the previous study by Petroz et al and Vilo et al. Both these studies concluded that both adults and pediatric population have the same pharmacokinetics.¹⁰

Potts et al concluded in his study that clearance of dexmedetomidine in neonates was approximately one – third of that of adults and reached the adult values by one year of age. Thus infusion rates should be lowered when the drug is used in infants. The dreaded side effects of dexmedetomidine, bradycardia and hypotension, was due to the blunting of the sympathetic nervous system.¹¹

Hammer et al studied the effect of dexmedetomidine on the cardiac electrical activity. He included 12 children in his study who were about to

undergo ablation of the supraventricular accessory pathway. The administration of the drug with the previous recommended doses resulted in significant decrease in heart rate and transient hypertension. Both the SA node and AV node were involved. Thus, the use of dexmedetomidine for study of the cardiac electrical activity was not recommended.¹²

Tobias et al in his study cited the use of therapeutic hypothermia as an added potential factor in two children who developed clinically significant bradycardia after the administration of dexmedetomidine infusion. Both the children recovered once the induced hypothermia was ceased. Hypotension and bradycardia caused by dexmedetomidine is offset by reduced dose and intravenous fluids administration.¹³

Mason et al In his study in 2008, mason et al studied dexmedetomidine in high doses as a sole sedative for children in MRI suite. He included 747 children with a loading dose of 2-3 microgm/kg followed by maintenance infusion of 1-2 mcg/kg/hr. Adequate sedation was achieved in 97 percent and bradycardia reported in 13 percent of subjects. However, none of them required treatment for bradycardia. The same authors later reported that three cases of significant bradycardia, who required intervention. Thus, the use of high dose dexmedetomidine is associated with adverse hemodynamic effects.¹⁴

In the same year, **Erkonen et al** reported a case where high dose dexmedetomidine produced hypertension in a child with traumatic brain injury.

Hypertension subsided once the infusion rates was lowered without discontinuation of the drug.¹⁵

Tobias et al in **2002** initially used dexmedetomidine to study its effects in pediatric patients. He did his study in four patients. Two patients on ventilators, one during surgery and the other undergoing a medical procedure. The infusion rates were between 0.2 – 0.7 microgm/kg/hr. There was mild bradycardia and hypotension in three children which did not require any treatment. Sedation was satisfactory in all except the one who underwent a medical procedure, who needed other sedatives to complete the procedure.¹⁶

The same author a year later demonstrated its effects in additional five pediatric patients. The degree of sedation was adequate in all the patients without any additional sedatives. These studies thus paved the way for its use as a newer sedative in pediatric patients.¹⁷

In **2004**, he still pioneered to compare the effects of dexmedetomidine with midazolam in children on mechanical ventilators. In this randomized control study where three groups were formed namely the midazolam group, group with low dose dexmedetomidine(0.25 microgm/kg) and the group with high dose dexmedetomidine(0.5 microgm/kg). The sedation scoring tools which were used are “The Ramsay sedation Score”, “Pediatric intensive care unit (PICU) sedation score” and a “score assessing the response to tracheal suctioning”. The “Bispectral Index Monitor(BIS)” was used to assess the awareness in addition. There was no statistically significant difference in the sedation and BIS scores

in all the three groups. Deficiently sedated patients were more in the midazolam group compared with the other two groups which received dexmedetomidine. Based on these observation they suggested that dexmedetomidine can be used as a better alternative to midazolam for sedating pediatric patients.¹⁸

Berkenbosch et al later found significant advantage of dexmedetomidine as a procedural sedative in a prospective analysis in children undergoing MRI, EEG or “nuclear medicine study” or combination of all. A quarter of the patients in the study had neurological disorder. They thus adjudged dexmedetomidine to be a safe and effective drug for procedural sedation.²¹ Similar reports were seen in another study conducted by Koroglu et al.²²

There are 2 studies which compared dexmedetomidine with propofol as an alternative for sedating patients undergoing MRI. Both of the studies validated dexmedetomidine as a suitable alternative for procedural sedation.^{23,24}

Walker et al was the first person who used dexmedetomidine for sedating pediatric patients with burns. He reported in his study that all the patients were adequately sedated based on clinical assessment. He also found that those patients who were not adequately sedated with other drugs such as opioids and benzodiazepines, were sedated well with dexmedetomidine.¹⁹

Czaja et al studied the effect of dexmedetomidine in patients in pediatric ICU. The therapy was adjusted based on “COMFORT” scores by including

signs and symptoms of both pain and agitation . The study concluded that the use of dexmedetomidine allowed reductions in the doses of opioids and benzodiazepines for most patients, but the close hemodynamic monitoring was mandatory to identify its adverse effects.²⁰

Two case reports mentioned the use of dexmedetomidine in sedating children in various settings. Dexmedetomidine's use was documented in “awake fiberoptic intubation, “awake craniotomy”, “sevoflurane anaesthesia” and radiosurgery. Its use in opioid and benzodiazepines withdrawal and vomiting is also reported.^{25,26}

He et al made a meta analysis of randomized controlled trials of dexmedetomidine which was used as an alternative to opioids fentanyl and morphine in children undergoing adenotonsillectomy surgeries. The “Cochrane Central Register of Controlled trials” and Medline was browsed. The parameters of analysis included number of patients who required rescue opioids in PACU, patients with Emergence agitation, Patients with PONV, time for eye opening and and time for extubation. Most of the parameters showed no statistical significance , but the time to eye opening and extubation was significantly decreased in the dexmedetomidine group. The analysis finally concluded that efficacy of dexmedetomidine, as postoperative analgesic and in prevention of emergence agitation, was equal to that of the opioids.²⁹

Zhuang et al studied the effect of dexmedetomidine as an analgesic and on respiration in patients undergoing tonsillectomy surgeries with OSAS. The

study was double blinded and randomized into 2 groups. One group received dexmedetomidine(1 microgm/kg) and the other group received morphine(100 microgm/kg). ETCO₂, “Children’s Hospital of Eastern Ontario Pain Scale score” and the rescue morphine doses were all monitored every fifteen minutes. The results showed that the respiratory depression caused by dexmedetomidine was less compared to morphine, but analgesia was poor.²⁷

The most recent study in **2014** by **Wang et al** evaluated the use of intranasal dexmedetomidine for cardiac and arousal attenuation in pediatric patients during intubation. Two groups were randomized who received dexmedetomidine (1 microgm/kg and 2 microgm/kg respectively) at least 30 minutes before intubation. The variables measured were behavior scores, sedation and mask induction scores. There was no difference in hemodynamic parameters among the two group, but the response to intubation was less in the group which received 2 microgm/kg of dexmedetomidine. The study thus introduced the new route of administration of dexmedetomidine for blunting intubation response.³³

Oloutye et al compared the effect of dexmedetomidine on postoperative sedation, postoperative pain and hemodynamics in children undergoing adenotonsillectomy. The subjects were randomized into four groups with two groups receiving dexmedetomidine and other two receiving morphine in different doses. The time for rescue opioid dose in group which received high dexmedetomidne and morphine was long when compared with the other

groups. Also, the number of patients who received more than one rescue opioid dose was high in these groups. Significant bradycardia was also reported in dexmedetomidine group during initial thirty minutes.²⁸

Pestieau et al did a similar study between dexmedetomidine and fentanyl in children undergoing adenotonsillectomy surgeries. Compared to the previous studies high dose dexmedetomidine (2 microg/kg and 4 microg/kg) were used. It was found that children belonging to the dexmedetomidine group had prolonged opioid free interval. However, the duration of stay in PICU was prolonged in dexmedetomidine groups. Thus, dexmedetomidine was found to spare rescue opioid doses and prevent respiratory depressive effects of opioids.³⁰

Patel et al used dexmedetomidine in OSAS patients coming for adenotonsillectomy to reduce the postoperative opioid requirements and reduce the emergence agitation seen in these patients. In one group, bolus of fentanyl was administered. In another group, dexmedetomidine infusion was given. Pain scores were assessed using objective scores. Emergence agitation was assessed using “PAED scale” and “5 point scale described by Cole”. The mean blood pressure and heart rate was low in dexmedetomidine group compared to fentanyl group. Emergence agitation was also not seen in dexmedetomidine group. The need for postoperative rescue opioid, emergence agitation and children with desaturating episodes was significantly less in dexmedetomidine

group. The results were convincing which asked for the use of dexmedetomidine in place of opioids for tonsillectomy surgeries.³¹

Gueler et al first initiated the study of dexmedetomidine in preventing emergence agitation which was commonly seen in children who underwent tonsillectomy surgeries. It was a randomized controlled study of sixty patients divided into 2 groups. The Study group received dexmedetomidine of 5 microgm/kg towards the end of surgery. Of note in all patients anaesthesia was induced and maintained with Sevoflurane, which pointed the association of Sevoflurane with emergence agitation. The emergence agitation and pain scores were better in the dexmedetomidine group. The time for eye opening and extubation was prolonged in dexmedetomidine group.³²

Meng et al did a similar type of study the effect of dexmedetomidine in reducing Emergence agitation in adenotonsillectomy patients with Sevoflurane anaesthesia. A total of 120 pediatric patients were randomized into 3 group, two of which received dexmedetomidine(either 1 microgm/kg or 0.5 microgm/kg) and one placebo group. All patients received iv midazolam as a premedicant to allay anxiety first followed by dexmedetomidine. Intraoperatively Heart rate, blood pressure and saturation was calculated, which continued in PACU also. At PACU, pain was assessed using “Visual Analogue Score” and sedation using “Ramsay sedation Score”. There was significantly less number of patients in the dexmedetomidine groups with Emergence agitation compared to the placebo group. Also, the time for eye opening and

extubation was increased, the sedation and pain scores were better in dexmedetomidine groups.³⁶

The latest study by **Hauber et al** also found similar reports of decreased incidence of Emergence agitation when dexmedetomidine was given as a rapid bolus in pediatric anaesthesia.³⁴

A study by **Mizrak et al** also hypothesized additional advantage of dexmedetomidine in reducing intraoperative blood loss in pediatric patients undergoing adenotonsillectomy.³⁵

MATERIALS AND METHODOLOGY

Type of Study – A prospective, Randomised double blind study

Place of study – Speciality Operation Theatre in Govt. Mohan Kumaramangalam medical college and Hospital.

Subjects – 62 Pediatric patients undergoing Adenotonsillectomy between age group 4 – 8 yrs of age. All patients belonged to the inpatient ward of ENT.

Materials – Philips MP 40 monitor, Dexmedetomidine ampoules, Fentanyl ampoules, Sevoflurane.

Inclusion Criteria

- ✓ American Society of Anesthesiologists physical status class I-II
- ✓ Aged 4-8 years

Exclusion Criteria

- ✓ BMI > 95 th percentile for age
- ✓ ASA III or more
- ✓ Sleep disorders
- ✓ Neurological disorders
- ✓ Hepatic/kidney dysfunction
- ✓ Congenital disorders

Patients will be randomly allocated to one of two groups namely, Dexmedetomidine group (1mcg/kg)(Group D) and Fentanyl group (2mcg/kg)(Group F). Randomization was done by asking the patient to pick up lots. When the patient fit into the inclusion criteria, he /she was asked to pick up the lots by a nurse , who is not included to the study.

Iv access was secured in the ward under parental guidance. One hour prior to surgery all patients will receive syrup Triclofos 75mg/kg per oral. On table preinduction monitors include HR,NIBP and SPO 2 and all basal readings were noted. Oxygen was given through Face mask 4l/min flow. Premedication was Glycopyrrolate 10 mcg/kg.

Group D received Dexmedetomidine 1mcg/kg as an infusion for 10 minutes. Group F received fentanyl 2mcg/kg. The study drug was administered by theatre assistant nurse, who is not included in the study.

They will be preoxygenated with 100 % oxygen and induced with IV Propofol 2mg/kg followed by inj succinylcholine 1.5mg/kg .Patient is then intubated nasally with appropriate endotracheal tube and maintained with mask O₂+N₂O(1:1)+Sevoflurane 2% via closed circuit with atracurium 0.3 mg/kg loading dose and 0.1mg/kg as supplemental dose every 15 min. The time at which inhalational agent is stopped before end of procedure is noted.

Intraoperatively, 0.9 Normal saline was given as fluid replacement and for maintenance.

At the end of procedure, the patient is reversed with neostigmine (40 microgm/kg) and glycopyrrolate(10 microgm/kg).

The time since stoppage of inhalation agent to eye opening and extubation are recorded and shifted to recovery room

The following variables are measured

1).Heart rate – measured for every 5 mins from premedication until 30 mins after than every 10 mins thereafter.

2).Blood pressure (SBP, DBP, MBP) – measured for every 5 mins from premedication until 30 mins than every 10 mins thereafter.

Bradycardia(<60/min) will be treated with atropine (10-20 mcg/kg)

3).”Ramsay sedation score” and “Children’s Hospital of Eastern Ontario Pain Scale score” were recorded in the recovery room at five minute interval for the first fifteen minutes. Later it was recorded every fifteen minutes.. Patients with CHEOPS score >8 received iv fentanyl 0.5 mcg/kg till the score at 15 min interval until the score is < 8.The total duration of surgery, time for opioid rescue dose and the total opioid needed are plotted.

4). Patients with Emergence agitation and those had nausea and vomiting was also noted.

5).They were discharged from PACU in the evening when the Aldrette score was more than more than 9 and were free from pain, nausea or vomiting.

STATISTICAL ANALYSIS

Outcomes measured were as following

Primary Outcome was the total dose of fentanyl as rescue opioid needed as postoperative analgesic in PACU.

Secondary Outcomes included

- Heart rate
- Systolic Blood Pressure
- Diastolic Blood pressure
- "Cheops and Ramsay sedation scores"
- Emergence agitation
- Nausea and Vomiting.

Categorical data (e.g., sex distribution, ASA physical status) will be analysed using the Pearson's Chi-square test . Parametrical numerical data between groups will be calculated by the Student's t-test. Within group variables, at different time points were analysed using the "Friedman's analysis of variance" (ANOVA) analysis. Microsoft excel and IBM SPSS (Statistical Package for Social Sciences) version 21 were used for statistical analysis.

A $P < 0.05$ is considered to be statistically significant and < 0.01 was highly significant.

“RAMSAY SEDATION SCORE”

If Awake

Ramsey 1

Anxious, agitated, restless

Ramsey 2

Cooperative, oriented, tranquil

Ramsey 3

Responsive to commands only

If Asleep

Ramsey 4

Brisk response to light glabellar tap or loud auditory stimulus

Ramsey 5

Sluggish response to light glabellar tap or loud auditory stimulus

Ramsey 6

No response to light glabellar tap or loud auditory stimulus

“CHEOPS SCORE”

Item	Behavioral		Definition
Cry	No cry	1	Child is not crying
	Moaning	2	Child is moaning or quietly vocalizing silent cry
	Crying	2	Child is crying, but the cry is gentle or whimpering
	Scream	3	Child is in a full-lunged cry; sobbing; may be scored with complaint or without complaint
Facial	Composed	1	Neutral facial expression
	Grimace	2	Score only if definite negative facial expression
	Smiling	3	Score only if definite positive facial expression
Child Verbal	None	1	Child not talking.
	Other complaints	1	Child complains, but not about pain, e.g., I want to see mummy or I am thirsty
	Pain complaint	2	Child complains about pain.
	Both complaints	2	Child complains about pain and about other things, e.g., It hurts; I want my mummy
	Positive	0	Child makes any positive statement or talks about other things without complaint.0
Torso	Neutral	1	Body (not limbs) is at rest; torso is inactive.
	Shifting	2	Body is in motion in a shifting or serpentine fashion
	Tense	2	Body is arched or rigid.
	Shivering	2	Body is shuddering or shaking involuntarily
	Upright	2	Child is in a vertical or upright position
	Restrained	2	Body is restrained
Touch	Not touching	1	Child is not touching or grabbing at wound
	Reach	2	Child is reaching for but not touching wound.
	Touch	2	Child is gently touching wound or wound area
	Grab	2	Child is grabbing vigorously at wound.
	Restrained	2	Child's arms are restrained
Legs	Neutral	1	Legs may be e in any position but are relaxed; includes gently swimming or separate-like movements
	Squirm/ kicking	2	Definitive uneasy or restless movements in the legs and /or striking out with foot or feet.
	Drawn up/tensed	2	Legs tensed and /or pulled up tightly to body and kept there
	Standing	2	Standing, crouching or kneeling
	Restrained	2	Child's legs are being held down

“ALDRETTE RECOVERY SCORE”

Activity	Respiration	Circulation	Consciousness	Oxygen Saturation
2: Moves all extremities voluntarily/ on command	2: Breaths deeply and coughs freely.	2: BP + 20 mm of preanesthetic level	2: Fully awake	2: Spo2 > 92% on room air
1: Moves 2 extremities	1: Dyspneic, shallow or limited breathing	1: BP + 20-50 mm of preanesthetic level	1: Arousable on calling	1: Supplemental O2 required to maintain Spo2 > 90%
0: Unable to move extremities	0: Apneic	0: BP + 50 mm of preanesthetic level	0: Not responding	0: Spo2 < 92% with O2 supplementation

RESULTS AND OBSERVATION

The comparative study between the 2 groups namely the fentanyl group and dexmedetomidine group was carried in 62 patients between 4-8 yrs of age. The following observations were made.

Results:

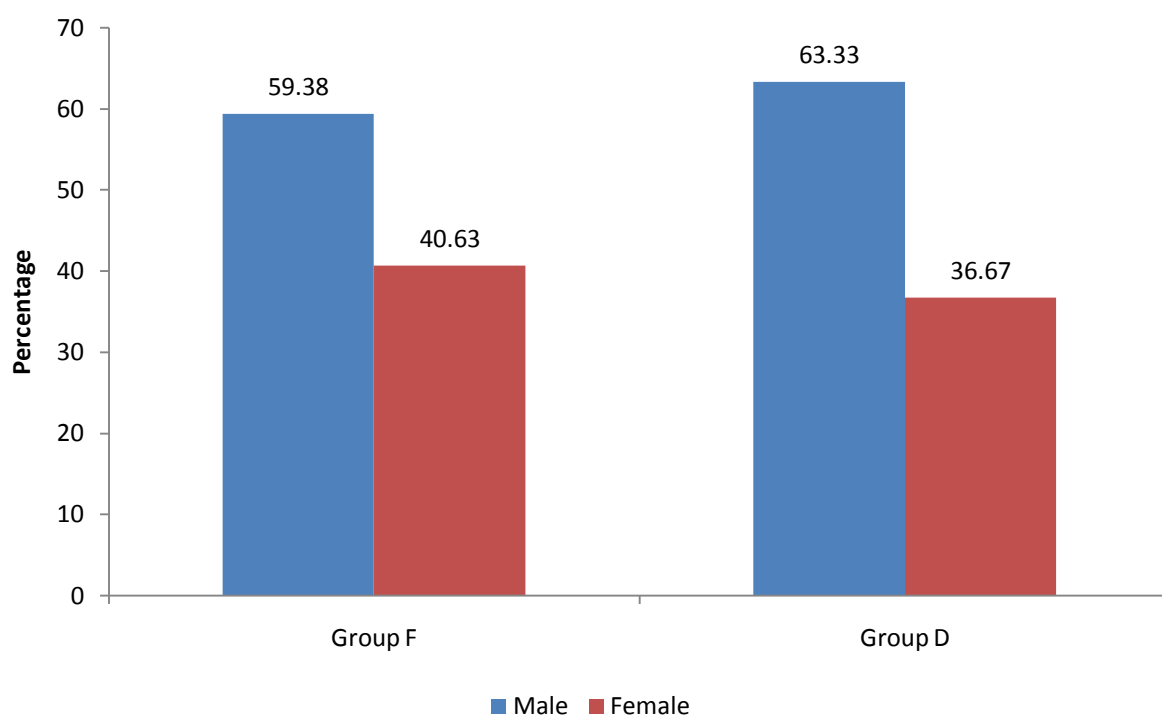
A total of 62 patients were included in the final analysis. Out of the 62 , 32 were randomized into group F and 30 were randomized into group D . Group F was given Fentanyl 2 mcg/kg. and Group D received Dexmedetomidine 1 mcg/kg after intubation according to the methodology described above.

In Group F, there were 19 males(59.38) and females(40.63). In Group D, there were 19 males(63.33) and 11 females(36.67).

There was no significant difference in gender between the 2 groups.

SEX DISTRIBUTION:

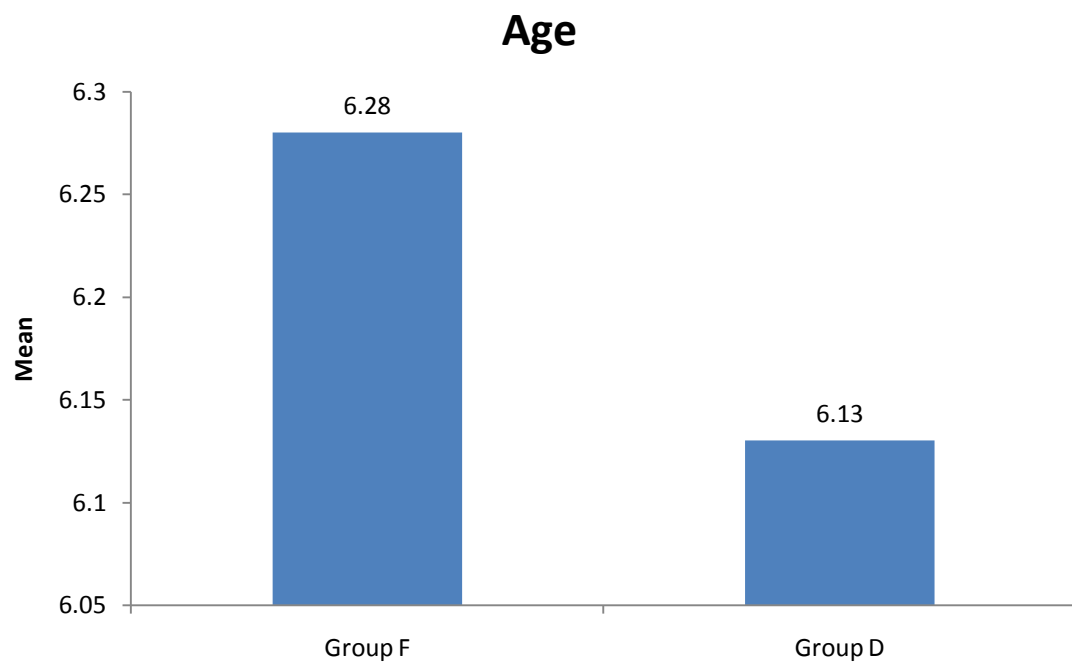
Group	Sex				Total
	Male		Female		
	N	%	N	%	
Group F	19	59.38	13	40.63	32
Group D	19	63.33	11	36.67	30
Total	38	61.29	24	38.71	62



AGE DISTRIBUTION:

Age	N	Mean	SD	t	p
Group F	32	6.28	1.17	0.55	0.586
Group D	30	6.13	0.94		

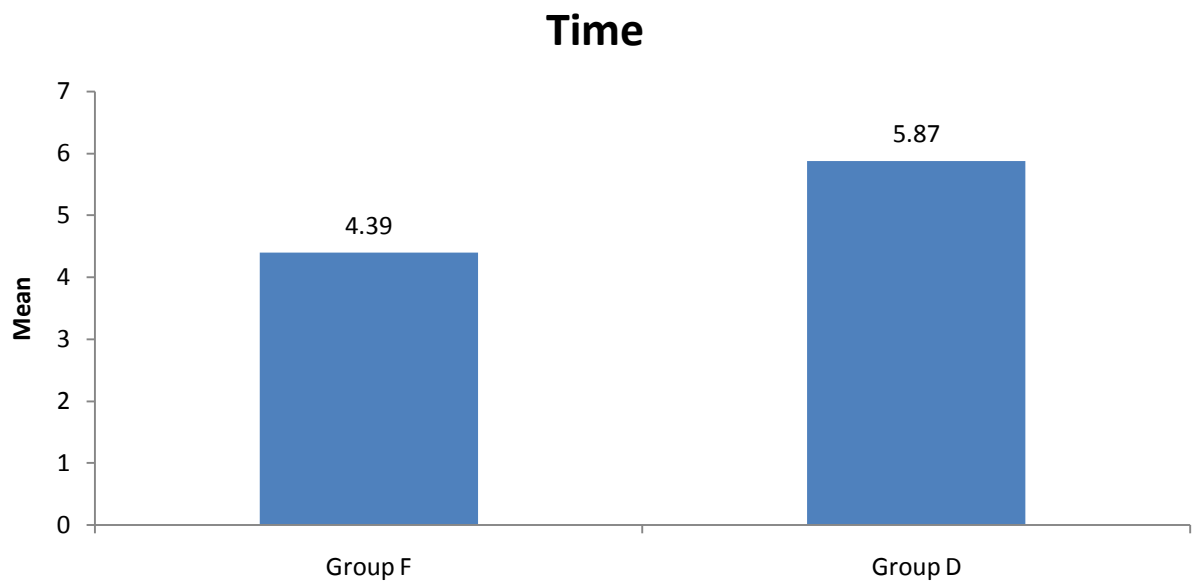
There is no statistical difference between the two groups in terms of age of the patient as p Value was more than >0.05



TIME FOR EYE OPENING AND EXTUBATION SINCE STOPPAGE OF SEVOFLURANE

Time for Eye opening	N	Mean	SD	t	p
Group F	32	4.39	0.96	6.96	< 0.001**
Group D	30	5.87	0.68		

** Significant at 1 %



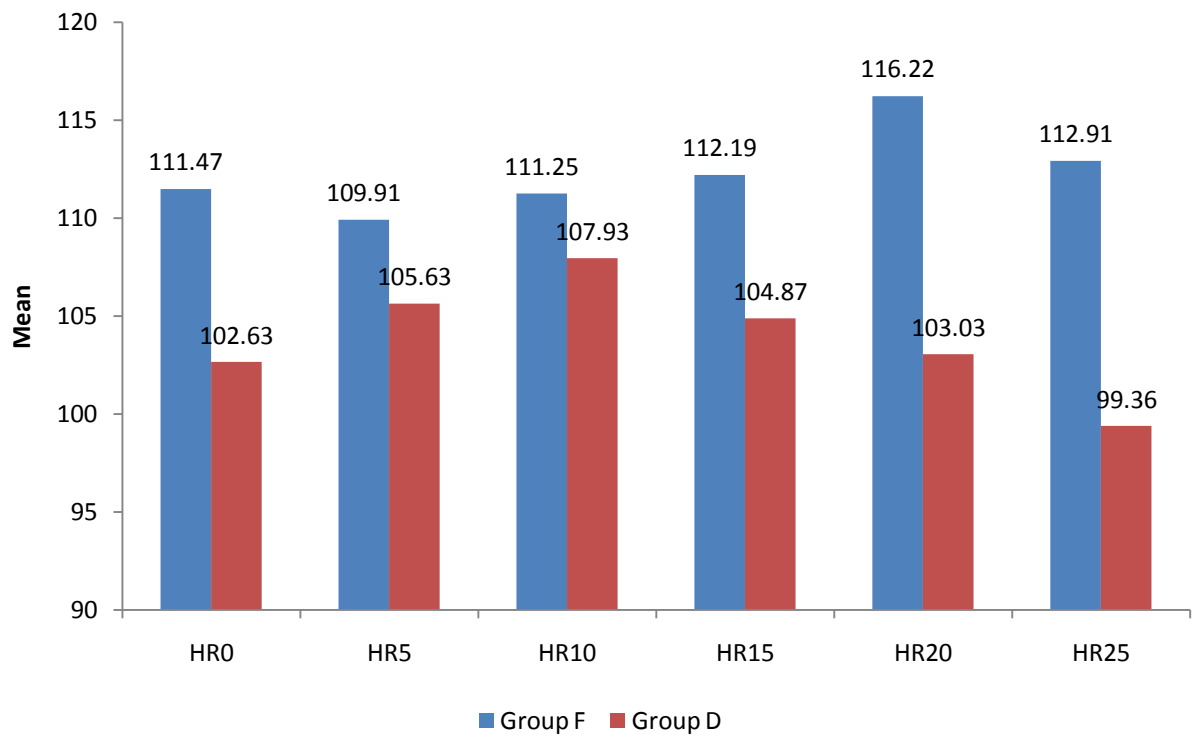
The time for eye opening was significantly higher in dexmedetomidine group compared to that of the fentanyl group

HEART RATE

	Group	N	Mean	SD	t	p
HR0	Group F	32	111.47	6.65	5.52	< 0.001**
	Group D	30	102.63	5.91		
HR5	Group F	32	109.91	5.35	2.73	0.008**
	Group D	30	105.63	6.93		
HR10	Group F	32	111.25	7.27	1.72	0.092
	Group D	30	107.93	7.96		
HR15	Group F	32	112.19	7.39	3.94	< 0.001**
	Group D	30	104.87	7.24		
HR20	Group F	32	116.22	8.97	6.63	< 0.001**
	Group D	30	103.03	6.39		
HR25	Group F	22	112.91	7.09	5.49	< 0.001**
	Group D	11	99.36	5.71		

** Significant at 1 %

There was significant difference in Heart rate between the 2 groups at various intervals except at 10 minute. The dexmedetomidine group showed significant reduction in heart rate compared to the fentanyl group.

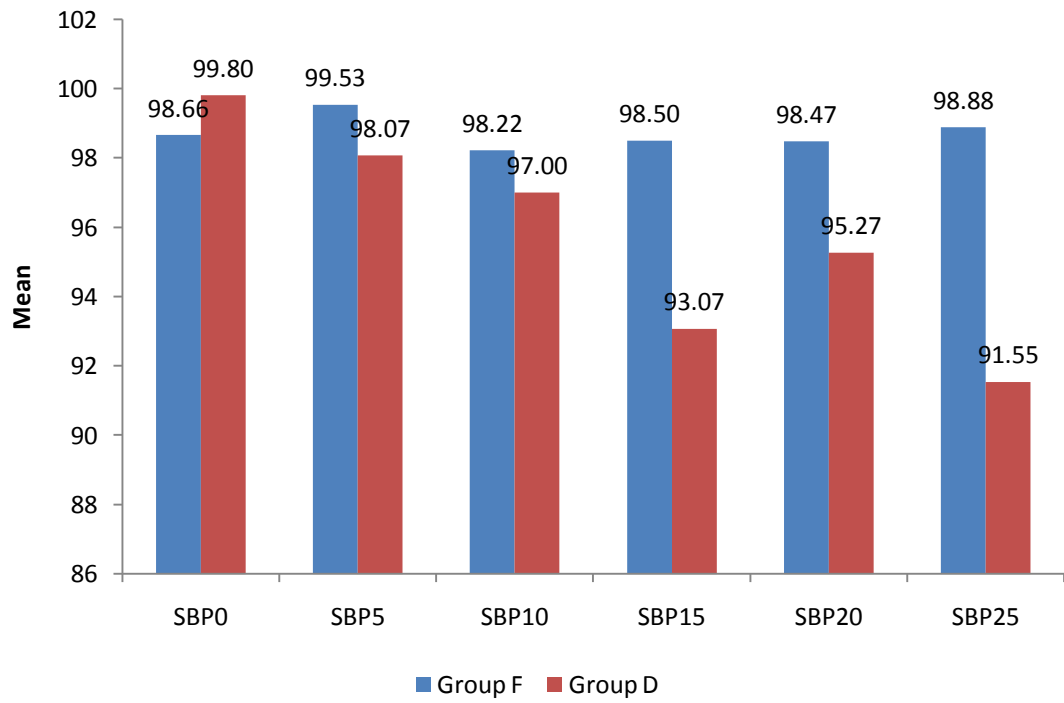


SYSTOLIC BLOOD PRESSURE

	Group	N	Mean	SD	t	p
SBP0	Group F	32	98.66	7.81	0.66	0.513
	Group D	30	99.80	5.62		
SBP5	Group F	32	99.53	7.87	0.88	0.382
	Group D	30	98.07	4.72		
SBP10	Group F	32	98.22	7.52	0.74	0.460
	Group D	30	97.00	5.07		
SBP15	Group F	32	98.50	6.91	3.24	0.002**
	Group D	30	93.07	6.24		
SBP20	Group F	32	98.47	6.22	2.30	0.025*
	Group D	30	95.27	4.53		
SBP25	Group F	25	98.88	5.34	3.80	0.001**
	Group D	11	91.55	5.32		

** Significant at 1 %

The systolic blood pressure in group D was lower everywhere except the first reading with statistical significance at 15, 20 and 25 th minute compared to that of the dexmedetomidine group.

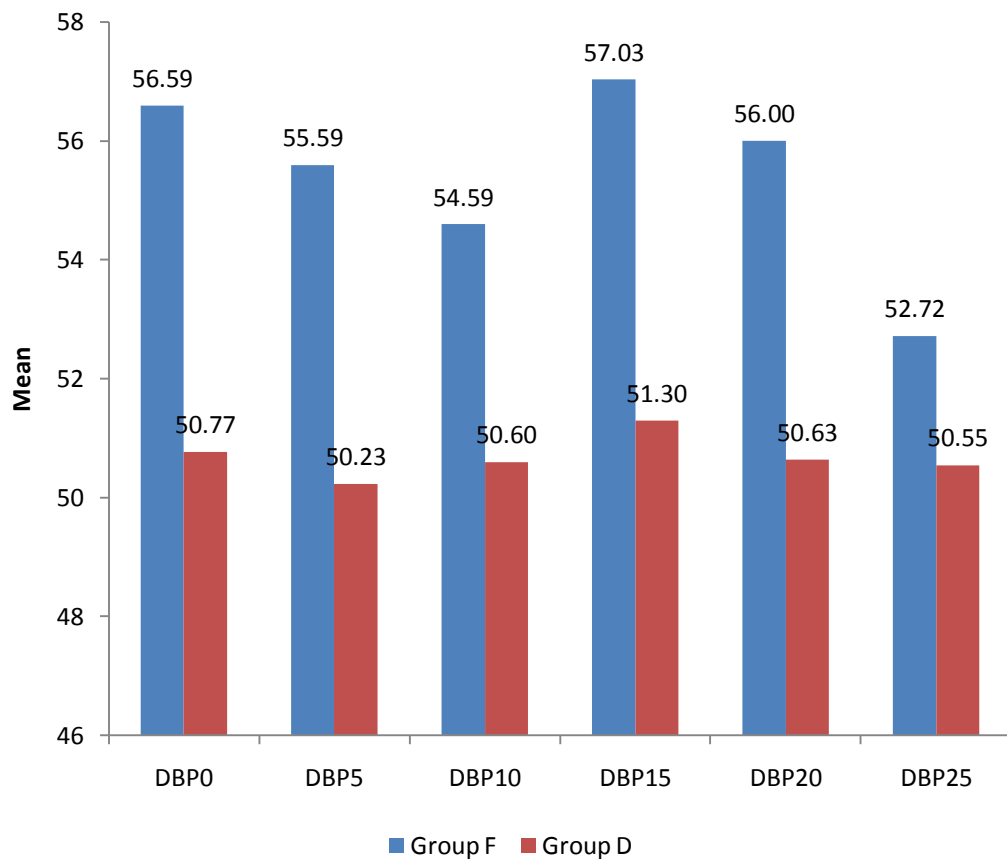


DIASTOLIC BLOOD PRESSURE

	Group	N	Mean	SD	t	p
DBP0	Group F	32	56.59	5.98	3.70	< 0.001**
	Group D	30	50.77	6.41		
DBP5	Group F	32	55.59	5.95	3.21	0.002**
	Group D	30	50.23	7.16		
DBP10	Group F	32	54.59	6.87	2.40	0.020*
	Group D	30	50.60	6.20		
DBP15	Group F	32	57.03	4.63	4.45	< 0.001**
	Group D	30	51.30	5.50		
DBP20	Group F	32	56.00	7.51	3.14	0.003**
	Group D	30	50.63	5.76		
DBP25	Group F	25	52.72	7.46	0.86	0.396
	Group D	11	50.55	5.72		

** Significant at 1 %

The Diastolic blood pressure was lower in Group D compared with that of Group F with statistically significant at all intervals except 25 th minute

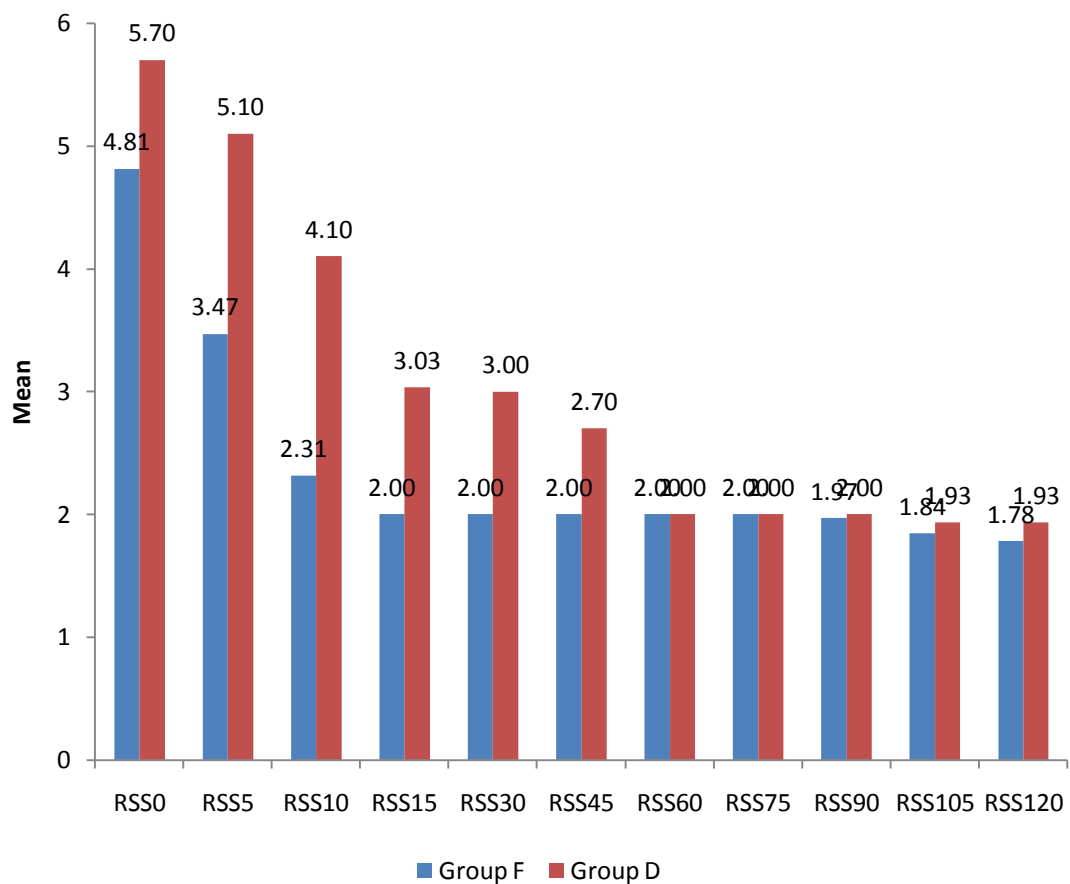


RAMSAY SEDATION SCORE

	Group	N	Mean	SD	t	P
RSS0	Group F	32	4.81	0.47	7.45	< 0.001**
	Group D	30	5.70	0.47		
RSS5	Group F	32	3.47	0.62	12.98	< 0.001**
	Group D	30	5.10	0.31		
RSS10	Group F	32	2.31	0.47	17.61	< 0.001**
	Group D	30	4.10	0.31		
RSS15	Group F	32	2.00	0.00	32.03	< 0.001**
	Group D	30	3.03	0.18		
RSS30	Group F	32	2.00	0.00	-	-
	Group D	30	3.00	0.00		
RSS45	Group F	32	2.00	0.00	8.50	< 0.001**
	Group D	30	2.70	0.47		
RSS60	Group F	32	2.00	0.00	-	-
	Group D	30	2.00	0.00		
RSS75	Group F	32	2.00	0.00	-	-
	Group D	30	2.00	0.00		
RSS90	Group F	32	1.97	0.18	0.97	0.337
	Group D	30	2.00	0.00		
RSS105	Group F	32	1.84	0.37	1.11	0.273
	Group D	30	1.93	0.25		
RSS120	Group F	32	1.78	0.42	1.71	0.092
	Group D	30	1.93	0.25		

** Significant at 1 %

The Ramsay Sedation Score in both groups started to regress as time progressed. However the scores in group D was significantly high during initial minutes of monitoring compared to that of Group F. After 45 minutes of monitoring there score of both groups were more or less the same and comparison becomes insignificant.

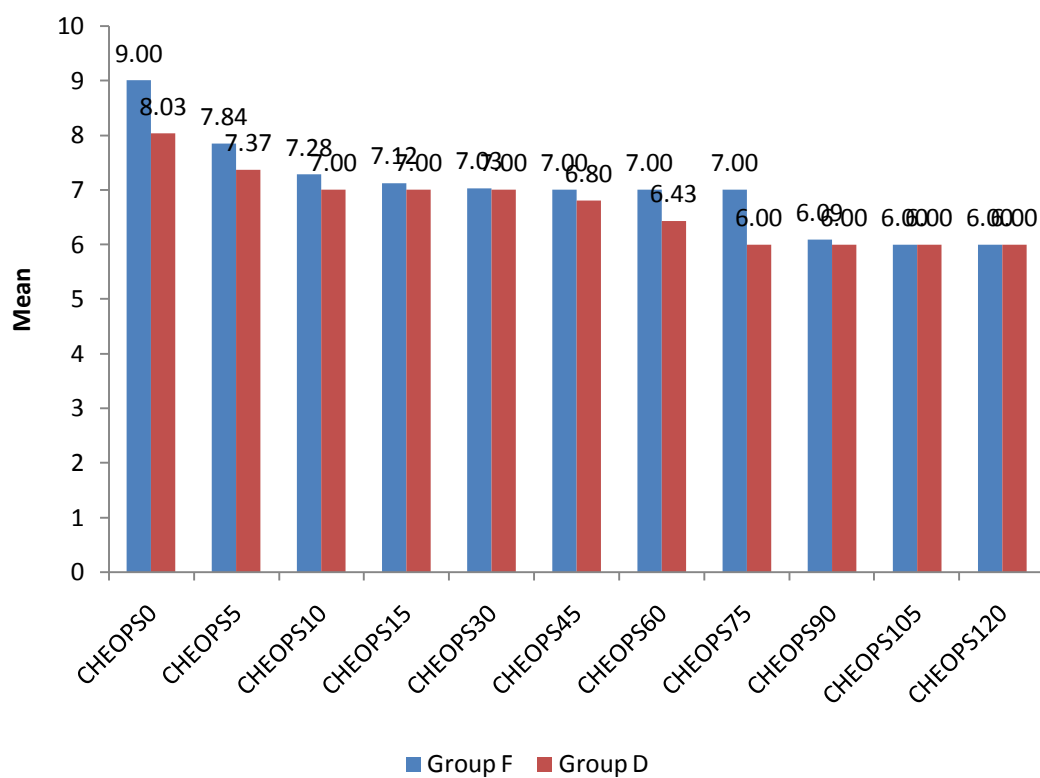


CHEOPS SCORE

	Group	N	Mean	SD	t	P
CHEOPS0	Group F	32	9.00	0.72	5.90	< 0.001**
	Group D	30	8.03	0.56		
CHEOPS5	Group F	32	7.84	0.81	2.79	0.007**
	Group D	30	7.37	0.49		
CHEOPS10	Group F	32	7.28	0.58	2.65	0.010**
	Group D	30	7.00	0.00		
CHEOPS15	Group F	32	7.13	0.49	1.39	0.169
	Group D	30	7.00	0.00		
CHEOPS30	Group F	32	7.03	0.18	0.97	0.337
	Group D	30	7.00	0.00		
CHEOPS45	Group F	32	7.00	0.00	2.78	0.007**
	Group D	30	6.80	0.41		
CHEOPS60	Group F	32	7.00	0.00	6.36	< 0.001**
	Group D	30	6.43	0.50		
CHEOPS75	Group F	32	7.00	0.00	-	-
	Group D	30	6.00	0.00		
CHEOPS90	Group F	32	6.09	0.30	1.73	0.088
	Group D	30	6.00	0.00		
CHEOPS105	Group F	32	6.00	0.00	-	-
	Group D	30	6.00	0.00		
CHEOPS120	Group F	32	6.00	0.00	-	-
	Group D	30	6.00	0.00		

** Significant at 1 %

The CHEOPS SCORE was very high in Group F needing early rescue opioid doses in the PACU compared to that of Group D which was statistically significant.



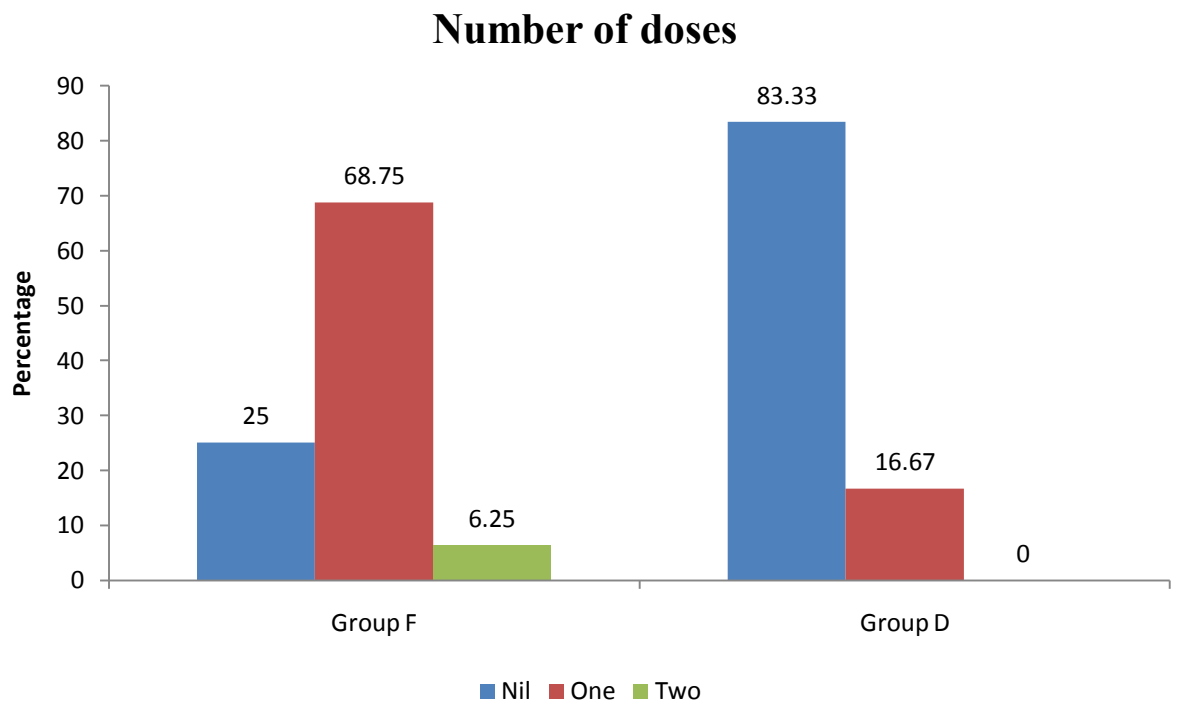
TOTAL RESCUE OPIOID DOSE

Group	Number of doses						Total	Chi square	p
	0		1		2				
	N	%	N	%	N	%			
Group F	8	25.00	22	68.75	2	6.25	32	21.42	< 0.001**
Group D	25	83.33	5	16.67			30		
Total	33	53.23	27	43.55	2	3.23	62		

** Significant at 1 %

Total no. of patients requiring rescue doses in Group F was high (24) compared to that of Group D, where only 5 patients required rescue doses. Among Group F, 22 patients required single opioid rescue and 2 patients required 2 doses.

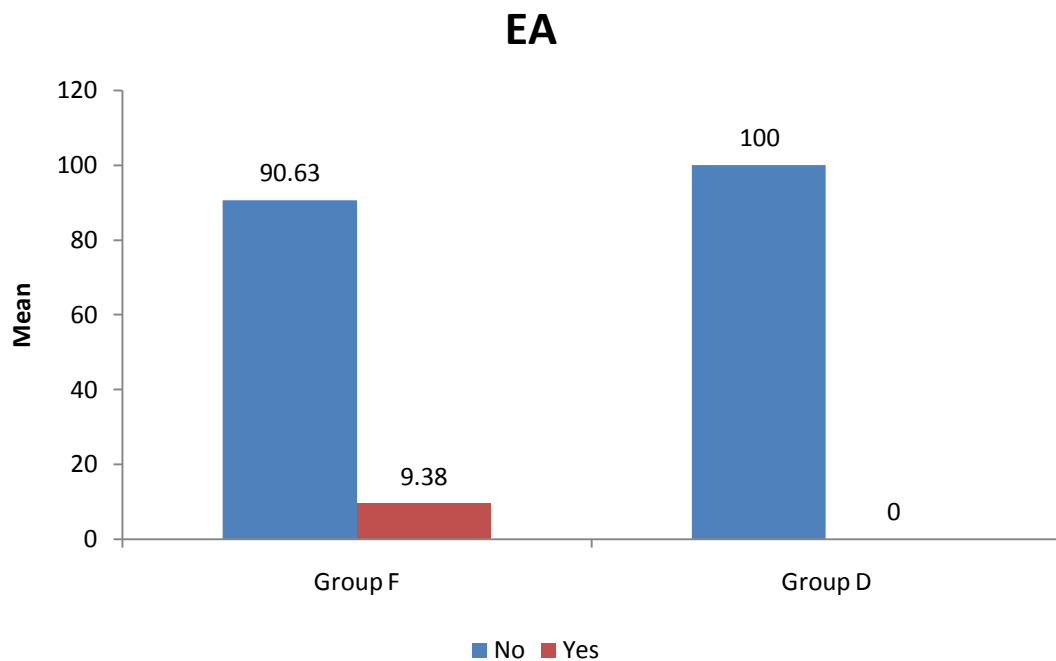
In Group D only 5 patients required single rescue dose.



EMERGENCE AGITATION

Group	EA				Total	Chi square	p
	No		Yes				
	N	%	N	%			
Group F	29	90.63	3	9.38	32	2.96	0.086
Group D	30	100.00			30		
Total	59	95.16	3	4.84	62		

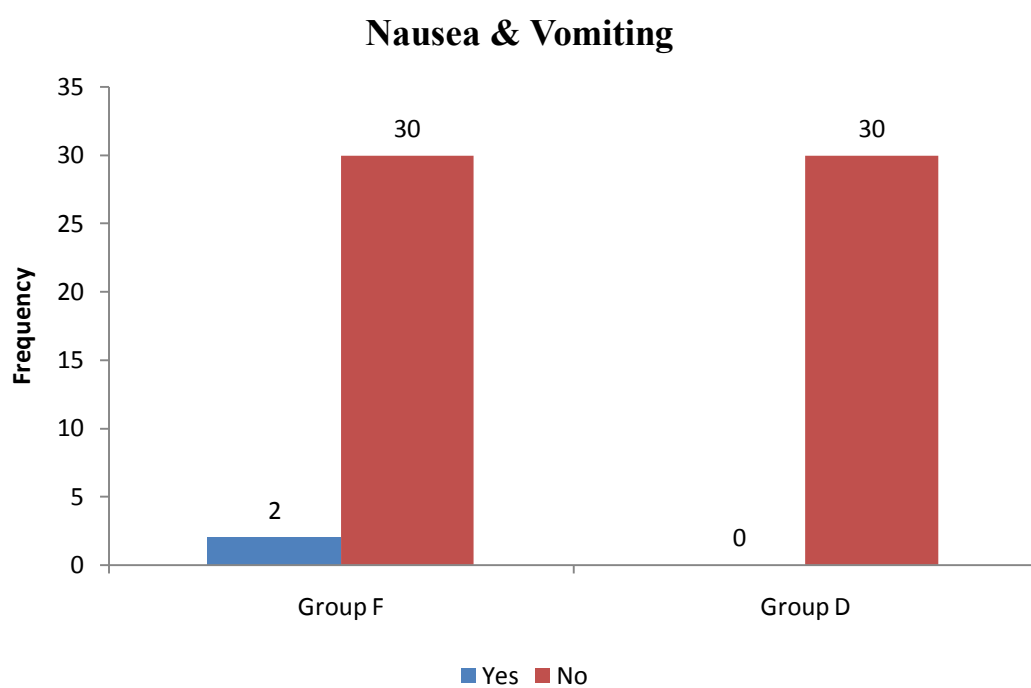
The incidence of Emergence agitation was reported in three cases of Group F, but it was not statistically significant



NAUSEA AND VOMITING

	Nausea & Vomiting		Chi square	p
	Yes	No		
Group F	2	30	1.94	0.164
Group D	0	30		

The incidence of Nausea and vomiting was reported in 2 cases of Group F



DISCUSSION

Post operative analgesia and sedation in pediatric anaesthesia has been one of the areas where management has been very difficult. Adenotonsillectomy surgeries are commonly performed in pediatric population where postoperative analgesia and sedation should be adequate since it is associated with high incidences of agitation and emergence delirium.

There are a variety of drugs and routes of administration available for post operative analgesia in pediatric population. But all are with their own side effects. NSAIDS are associated with high risk of post tonsillectomy bleeding. Opioids carry the risk of post operative respiratory depression, nausea and vomiting. All these have led to the use of newer drugs in management of pain and sedation in adenotonsillectomy patients.

We chose dexmedetomidine as an alternative to Opioids in the management of postoperative pain, sedation and prevention of emergence delirium. Dexmedetomidine is a α_2 agonist which is more potent than its precursor clonidine. Its uses are diverse and find its application in maintaining intraoperative hemodynamics, sedation and analgesia. The use of dexmedetomidine was initially restricted in adults for sedation in ICU. Later its offlabel use in pediatric patients was on the rise initially for ICU sedation and later for medical procedures. The pharmacokinetic study of the drug in children more than one year revealed similar values as in adults.

The sample size of the study was 62, which was derived from G * power 3.13 version and from the parent study. All the patients belonged to ASA category I between age group 4 – 8 yrs of age.

The dose of dexmedetomidine was chosen from previous studies done in adenotonsillectomy surgeries. The dexmedetomidine group received a dose of 1 microgm/kg. The fentanyl group received a dose of 2 mcg/kg.

The age distribution was comparable in our study, with the mean age being 6 years in both the groups and insignificant difference was noted ($p=0.536$) between the two groups. The gender difference between the groups was not significant. These show that any difference between the two groups in demographic profiles would occur only by chance.

The aim of study was to study the effect of dexmedetomidine in patients undergoing adenotonsillectomy surgeries with respect to intraoperative hemodynamics, postoperative pain, sedation and prevention of postoperative emergence delirium , nausea and vomiting.

The values of Heart rate were lower in dexmedetomidine group throughout the surgery compared to fentanyl with significance at all intervals except at 10th minute of monitoring(P value 0.092). Similar results have been found in previous study by Oloutye et al.

Systolic Blood Pressure was also better in dexmedetomidine group at 15 , 20 and 25 minutes of monitoring and was statistically significant (P value of

0.002,0.025,0.001). Diastolic Blood pressure was significant throughout except at 25 minutes of monitoring(P value – 0.396)

The Ramsay Sedation score decreased in both the groups in time. The values were statistically significant during initial minutes of monitoring. Later on the values were incomparable. Study by Olutye et al also demonstrated similar effects but there the results were not statistically significant. After 45 minutes of observation the Ramsay sedation score was 2 in both the groups.

The time since stoppage of the volatile and eye opening was increased in the dexmedetomidine group. This was also seen in studies by Meng et al and Gueler et al.

Emergence agitation was not seen in the dexmedetomidine group but was however was not significant when compared with the fentanyl group which reported only 2 cases. Various many studies have however given significance of dexmedetomidine in preventing Emergence agitation.^{31,32,33,36}

The incidence of nausea and vomiting was also not significant.

CONCLUSION

The study “The effect of Dexmedetomidine on hemodynamics ,postoperative analgesia and sedation in Pediatric patients undergoing adenotonsillectomy” thus concludes that the addition of dexmedetomidine in pediatric adenotonsillectomy patients has resulted in better intraoperative hemodynamics with no reports of bradycardia or hypotension. The need for postoperative “rescue opioid” was also significantly reduced by the use of this drug.

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The effect of Dexmedetomidine on hemodynamics ,postoperative Analgesia and sedation in Pediatric patients undergoing adenotonsillectomy

Name: Age : Sex:

Diagnosis: Procedure:

Asa status:

Premedication:Inj. Glycopyrolate 0.2mg IV

Test drug given in ten min

Induction: Inj. Propofol 2 mg/kg IV and Inj Sch 1.5 mg/kg IV

Maintenance: O2+N2O(1:1)+Sevoflurane 2%, atracurium 0.3 mg/kg LD and 0.1mg/kg MD 15 min

Time	5	10	15	20	25	30	40	50	60
HR									
SBP									
DBP									

The time since stoppage of inhalation agent to eye opening and extubation:

Time	5	10	15	30	45	60	75	90	105	120
RSS										
CHEOPS										

CHEOPS >8 give iv fentanyl 0.5 mg/kg as rescue dose

Emergence Agitation*: Present/Absent

Aldrete Score^:

RSS¹- Ramsay sedation score

CHEOPS"- Children Hospital eastern ontario pain scale

*Patients crying, restless, disoriented, unresponsive to the parent’s voice, with non purposeful thrashing movements requiring additional personnel to prevent bodily harm, and inconsolable even after parental presence, rescue analgesia and additional measures of comfort were considered to have Emergence agitation

S NO.	Name	Age	Sex	Group	Time	HR					SBP					DBP					RSS												CHEOPS												LA	Rescue Opioid		Nausea		
						0	5	10	15	20	25	0	5	10	15	20	25	0	5	10	15	20	25	0	5	10	15	30	45	60	75	90	105	120	0	5	10	15	30	45	60	75	90	105	120	Time	dose			
1	Ajmal	6 m	F	5	110	120	125	112	112			98	96	95	90	88		40	45	44	49	40		5	4	3	2	2	2	2	2	2	2	1	9	8	7	7	7	7	7	7	7	6	6	no	0 min	10 mcg	Yes	
2	Pradeep	6 m	F	6	116	114	124	111	141	133		88	80	100	98	90	98	56	55	49	60	66	60	4	2	2	2	2	2	2	2	2	2	2	8	7	7	7	7	7	7	7	7	6	6	no	nil			
3	Kumar	8 m	F	4	116	113	116	121	118	115		101	111	100	99	91	91	60	66	45	55	76	60	5	4	3	2	2	2	2	2	2	2	1	9	8	8	7	7	7	7	7	7	6	6	no	0min	12 mcg		
4	Savithri	5 f	F	4	120	109	115	110	99	111		99	91	90	94	88	98	49	52	54	60	61	54	5	4	3	2	2	2	2	2	2	1	1	1	10	9	9	9	7	7	7	7	6	6	6	no	0 min,15	22mcg	Yes
5	Dhanasekar	6 m	F	6	112	108	111	102	111	111		90	95	100	101	98	101	60	62	56	55	54	62	5	3	2	2	2	2	2	2	2	2	1	9	9	8	7	7	7	7	7	6	6	6	no	0 min	12 mcg		
6	Padmalakshmi	7 f	F	3	112	113	111	114	132	112		98	99	102	111	116	113	56	55	60	61	62	55	5	4	2	2	2	2	2	2	2	2	10	8	7	7	7	7	7	7	6	6	6	no	0 min	10 mcg			
7	Durga prasad	6 m	F	4	120	113	112	115	112	110		100	99	98	93	98	104	60	56	55	58	55	62	4	3	3	2	2	2	2	2	2	2	10	9	7	7	7	7	7	7	6	6	6	no	0 min	11 mcg			
8	Prasath	5 m	F	5	116	112	110	109	107	111		101	98	99	98	96	106	56	55	54	61	62	56	5	4	3	2	2	2	2	2	2	2	9	8	7	7	7	7	7	7	6	6	6	no	0 min	9 mcg			
9	Allen	8 m	F	4	100	101	111	120	113	98		98	112	110	108	98	103	65	60	65	56	55	55	5	3	2	2	2	2	2	2	2	2	10	9	9	9	8	7	7	7	6	6	6	no	0 min,15	25 mcg			
10	John C George	6 m	F	4	118	112	112	120	118	112		90	98	89	99	100	102	56	54	60	61	62	54	5	3	2	2	2	2	2	2	2	2	9	8	7	7	7	7	7	7	6	6	6	no	0 min	9 mcg			
11	Tennyson	7 m	F	4	112	110	112	113	117	110		90	112	98	112	101	100	62	56	55	54	60	65	5	3	2	2	2	2	2	2	2	2	9	9	7	7	7	7	7	7	6	6	6	no	0 min	8 mcg			
12	Vignesh	8 m	F	4	100	116	123	128	130	114		120	114	108	99	101	98	65	55	56	59	54	45	4	3	2	2	2	2	2	2	2	2	8	7	7	7	7	7	7	7	6	6	6	no	nil				
13	Balavenkat	4 m	F	6	102	112	114	112	110	108		98	96	88	84	87	99	45	43	47	49	52	64	5	4	2	2	2	2	2	2	2	2	10	7	7	7	7	7	7	7	6	6	6	no	0 min	12 mcg			
14	Kalyani	5 f	F	3	112	109	108	113	116	109		98	94	87	90	101	93	60	50	45	49	52	44	5	4	2	2	2	2	2	2	2	2	9	7	7	7	7	7	7	7	6	6	6	no	0 min	8 mcg			
15	Vidya devi	5 f	F	4	112	110	109	112	118	108		80	98	91	90	102	95	54	62	61	56	58	41	5	4	2	2	2	2	2	2	2	2	10	9	8	7	7	7	7	7	6	6	6	no	0 min	10 mcg			
16	Aldrin Joseph	5 m	F	3	112	101	115	121	109	111		98	99	101	102	100	95	52	62	65	55	45	41	4	4	2	2	2	2	2	2	2	2	9	9	7	7	7	7	7	7	6	6	6	no	0 min	15 mcg			
17	Durga	6 f	F	5	115	113	102	111	100	124		99	97	100	105	106	96	65	53	51	51	52	48	5	4	2	2	2	2	2	2	2	2	9	8	8	7	7	7	7	7	6	6	6	no	0 min	15 mcg			
18	Harish	7 m	F	6	102	100	104	100	126			98	90	100	108	101		54	62	61	66	65		4	4	2	2	2	2	2	2	2	2	8	7	7	7	7	7	7	7	6	6	6	no	nil				
19	Dhivya	6 f	F	2	100	109	118	117	121			90	99	90	99	98		55	45	47	52	51		5	3	2	2	2	2	2	2	2	2	8	7	7	7	7	7	7	7	6	6	6	no	nil				
20	Lakshmi	4 f	F	5	112	116	109	122	120			98	102	100	99	103		60	61	55	56	62		5	3	3	2	2	2	2	2	2	2	8	7	7	7	7	7	7	7	6	6	6	no	nil				
21	Gayathri	8 f	F	3	102	108	109	102	112			90	98	99	97	100		54	60	62	61	61		5	3	3	2	2	2	2	2	2	2	8	8	7	7	7	7	7	7	6	6	6	yes	nil				
22	Kishore	6 m	F	4	112	102	108	107	108			100	102	103	99	104		62	63	61	61	56		5	2	2	2	2	2	2	2	2	2	8	7	7	7	7	7	7	7	6	6	6	no	nil				
23	Madhu	6 f	F	4	119	109	108	108	112			110	90	98	99	91		55	46	44	63	54		4	3	2	2	2	2	2	2	2	1	1	10	9	8	7	7	7	7	7	6	6	6	no	0 min	11 mcg		
24	Keerthi	6 m	F	4	129	110	118	119	108	123		104	110	98	99	97	99	62	62	55	51	52	49	5	4	2	2	2	2	2	2	2	2	8	7	7	7	7	7	7	7	6	6	6	no	nil	12 mcg			
25	Anu rekha	8 f	F	4	108	108	107	109	124	112		111	98	99	95	101	110	56	61	65	62	54	45	5	4	2	2	2	2	2	2	2	2	9	7	7	7	7	7	7	7	6	6	6	yes	0 min	13 mcg			
26	Girija	6 f	F	5	110	107	104	103	121	107		112	101	123	100	98	100	55	54	45	55	65	54	5	4	2	2	2	2	2	2	2	2	9	8	7	7	7	7	7	7	6	6	6	no	0 min	9 mcg			
27	Immanuel	7 m	F	5	118	109	100	118	130	112		100	112	110	112	99	97	54	59	60	62	60	56	5	4	2	2	2	2	2	2	2	2	9	7	7	7	7	7	7	7	6	6	6	no	0 min	15 mcg			
28	Rishi	6 m	F	5	110	109	112	100	117	112		98	90	90	96	103	91	65	49	54	56	55	60	4	4	2	2	2	2	2	2	2	1	1	9	7	7	7	7	7	7	7	6	6	6	no	0 min	16 mcg		
29	Vijay anand	6 m	F	5	112	101	103	117	116	121		99	92	98	95	109	98	57	49	52	55	56	45	5	4	3	2	2	2	2	2	2	1	2	9	7	7	7	7	7	7	7	6	6	6	no	0 min	17 mcg	Yes	
30	Srireavathy	7 f	F	5	110	104	101	101	114			93	99	91	90	98	95	61	56	65	54	47	42	5	3	3	2	2	2	2	2	2	2	10	8	7	7	7	7	7	7	6	6	6	yes	0 min	10 mcg			
31	Saranya	7 f	F	5	110	119	100	103	110			103	104	98	103	91	96	55	55	54	65	45	51	5	3	2	2	2	2	2	2	2	1	2	9	8	7	7	7	7	7	7	6	6	6	no	0 min	14 mcg		
32	Dharun Prasant	7 m	F	5	108	120	129	120	117			105	109	90	88	97	94	45	56	45	57	43	50	6	3	3	2	2	2	2	2	2	1	9	8	7	7	7	7	7	7	6	6	6	no	0 min	10 mcg			

S.No.	Name	Age	Sex	Group	Time	HR					SBP					DBP					RSS												CHEOPS												EA	Rescue Opioid		Nausea		
						0	5	10	15	20	25	0	5	10	15	20	25	0	5	10	15	20	25	0	5	10	15	30	45	60	75	90	105	120	0	5	10	15	30	45	60	75	90	105	120		Time	dose		
1	Ranjith	6 m	D	6	100	101	112	102	99			100	90	88	86	88		50	48	49	50	61		6	5	4	4	3	2	2	2	2	2	2	8	8	7	7	7	7	7	6	6	6	6	no	nil			
2	Karthik	6 m	D	6	110	110	118	99	110			112	98	96	90	92		49	48	52	56	58		6	5	4	3	3	2	2	2	2	2	2	8	7	7	7	7	7	7	6	6	6	6	no	nil			
3	Bala ganesh	6 m	D	5	100	102	103	104	103			98	93	98	93	91		45	47	43	40	48		6	5	4	3	3	2	2	2	2	2	2	8	7	7	7	7	7	7	6	6	6	6	no	nil			
4	Vijay shankar	5 m	D	7	99	120	100	101	98			92	93	99	91	90		43	42	41	48	52		6	5	4	3	3	2	2	2	2	2	2	8	7	7	7	7	7	7	6	6	6	6	no	nil			
5	Suresh kumar	7 m	D	6	104	97	98	99	104			89	90	89	92	93		46	44	41	41	60		6	5	4	3	3	2	2	2	2	2	2	8	7	7	7	7	7	7	6	6	6	6	no	nil			
6	Lalitha	6 f	D	5	100	109	100	108	104	102	104	105	103	102	104	102	49	53	51	52	56	59	6	5	4	3	3	3	2	2	2	2	2	2	8	8	7	7	7	7	7	6	6	6	6	no	nil			
7	Keerthi	4 f	D	6	92	92	112	99	92	99	102	105	100	90	98	96	44	43	46	47	49	50	6	5	4	3	3	3	2	2	2	2	2	9	7	7	7	7	7	7	6	6	6	6	no	0 min	12 mg			
8	Ramesh	8 m	D	6	100	102	110	100	102	94	98	96	98	94	98	96	54	44	55	57	58	43	5	5	4	3	3	3	2	2	2	2	2	7	7	7	7	7	7	7	6	6	6	6	no	nil				
9	Usha	7 f	D	6	109	102	102	98	100	94	100	102	98	99	92	90	55	67	54	51	43	44	6	6	5	3	3	3	2	2	2	1	1	7	7	7	7	7	7	6	6	6	6	6	no	nil				
10	Senthamil selva	7 m	D	6	98	99	112	93	101	102	102	110	99	98	92	90	57	45	49	51	54	55	5	5	4	3	3	3	2	2	2	2	2	8	7	7	7	7	7	6	6	6	6	6	no	nil				
11	Mohammed	6 m	D	6	99	101	102	101	98			116	102	102	99	103		52	55	54	55	58		5	5	4	3	3	3	2	2	2	2	2	8	7	7	7	7	6	6	6	6	6	no	nil				
12	Nazima Begum	5 f	D	5	99	97	92	90	99			112	102	90	99	89		54	55	54	43	43		6	5	4	3	3	3	2	2	2	2	2	8	7	7	7	7	7	6	6	6	6	6	no	nil			
13	Jasmine	7 f	D	6	100	101	102	101	102			100	98	90	95	92		55	45	55	44	46		6	5	4	3	3	3	2	2	2	2	2	8	7	7	7	7	7	6	6	6	6	6	no	nil			
14	Indra	6 f	D	5	92	98	99	100	98			98	96	95	98	99		63	41	65	45	49		6	5	4	3	3	3	2	2	2	2	2	8	8	7	7	7	7	6	6	6	6	6	no	nil			
15	Megala	6 f	D	6	101	111	120	112	101	101	95	96	98	92	90	96	63	52	47	45	44	47	6	5	4	3	3	3	2	2	2	2	2	8	8	7	7	7	7	6	6	6	6	6	no	nil				
16	Ijaz	6 m	D	4	100	110	113	110	99	90	94	100	102	103	98	88	43	47	49	55	47	48	6	5	4	3	3	3	2	2	2	2	2	8	8	7	7	7	6	6	6	6	6	6	no	nil				
17	Sekar	6 m	D	7	100	108	107	100	104	101	103	98	98	89	99	86	46	57	45	59	49	44	6	5	4	3	3	3	2	2	2	2	2	8	8	7	7	7	7	6	6	6	6	6	no	nil				
18	Suresh	6 m	D	6	104	103	102	102	101	100	100	99	92	88	100	84	48	60	46	52	45	54	6	6	5	3	3	3	2	2	2	2	2	8	8	7	7	7	7	6	6	6	6	6	no	nil				
19	Selvam	6 m	D	6	102	101	110	112	106	112	98	99	89	85	98	89	44	40	49	53	46	55	5	5	4	3	3	3	2	2	2	2	2	7	8	7	7	7	7	6	6	6	6	6	no	nil				
20	Karthik	5 m	D	6	102	100	113	110	101	98	98	95	98	100	101	90	41	51	47	54	45	57	6	5	4	3	3	3	2	2	2	2	2	7	8	7	7	7	7	6	6	6	6	6	no	nil				
21	Tamilselvan	4 m	D	6	100	112	110	102	100			99	98	103	105	98		49	52	55	55	44		5	5	4	3	3	3	2	2	2	1	1	9	8	7	7	7	7	6	6	6	6	no	0 min	11mg			
22	Rajarajan	6 m	D	5	112	105	102	112	109			100	92	88	85	92		48	59	56	57	57		5	5	4	3	3	3	2	2	2	2	2	9	8	7	7	7	6	6	6	6	6	6	no	0 min	15mg		
23	Nedumaran	8 m	D	6	110	115	129	120	104			97	97	100	82	89		45	50	60	59	51		6	5	4	3	3	3	2	2	2	2	2	8	7	7	7	7	6	6	6	6	6	no	nil				
24	Amritha	6 f	D	5	102	118	112	113	102			95	93	101	80	99		41	54	54	52	51		6	5	4	3	3	3	2	2	2	2	2	9	7	7	7	7	6	6	6	6	6	no	0 min	18 mg			
25	Killi Valavan	7 m	D	6	112	100	103	102	103			98	97	102	90	98		56	58	47	51	55		6	5	4	3	3	3	2	2	2	2	2	9	7	7	7	7	6	6	6	6	6	no	0 min	11 mg			
26	Yasmine	7 f	D	6	118	114	112	102	109			98	92	104	92	95		55	43	45	53	43		6	5	4	3	3	3	2	2	2	2	2	8	7	7	7	7	6	6	6	6	6	no	nil				
27	Vinodh	7 m	D	7	112	110	110	110	100			100	102	102	96	99		53	46	51	56	47		5	6	5	3	3	2	2	2	2	2	8	7	7	7	7	6	6	6	6	6	no	nil					
28	Ruthra	6 f	D	6	100	106	121	111	101			102	100	100	94	93		59	49	66	55	49		6	5	4	3	3	2	2	2	2	2	8	7	7	7	7	6	6	6	6	6	no	nil					
29	Haricharan	6 m	D	7	102	111	110	115	129			99	102	98	88	90		62	67	48	59	51		5	5	4	3	3	2	2	2	2	2	8	7	7	7	7	6	6	6	6	6	no	nil					
30	Sumithra	6 f	D	6	100	114	102	118	112			95	102	90	97	98		54	45	44	44	60		5	5	4	3	3	2	2	2	2	2	8	7	7	7	7	6	6	6	6	6	no	nil					